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**Synthesis of Naturally Occurring and Synthetic
Acetylenes via Alkylidene Carbenoid Rearrangements**

by



Annabelle Liew Kiow Shi Shun

A thesis submitted to the Faculty of Graduate Studies and Research in
partial fulfillment of the requirements for the degree of Master of Science

Department of Chemistry

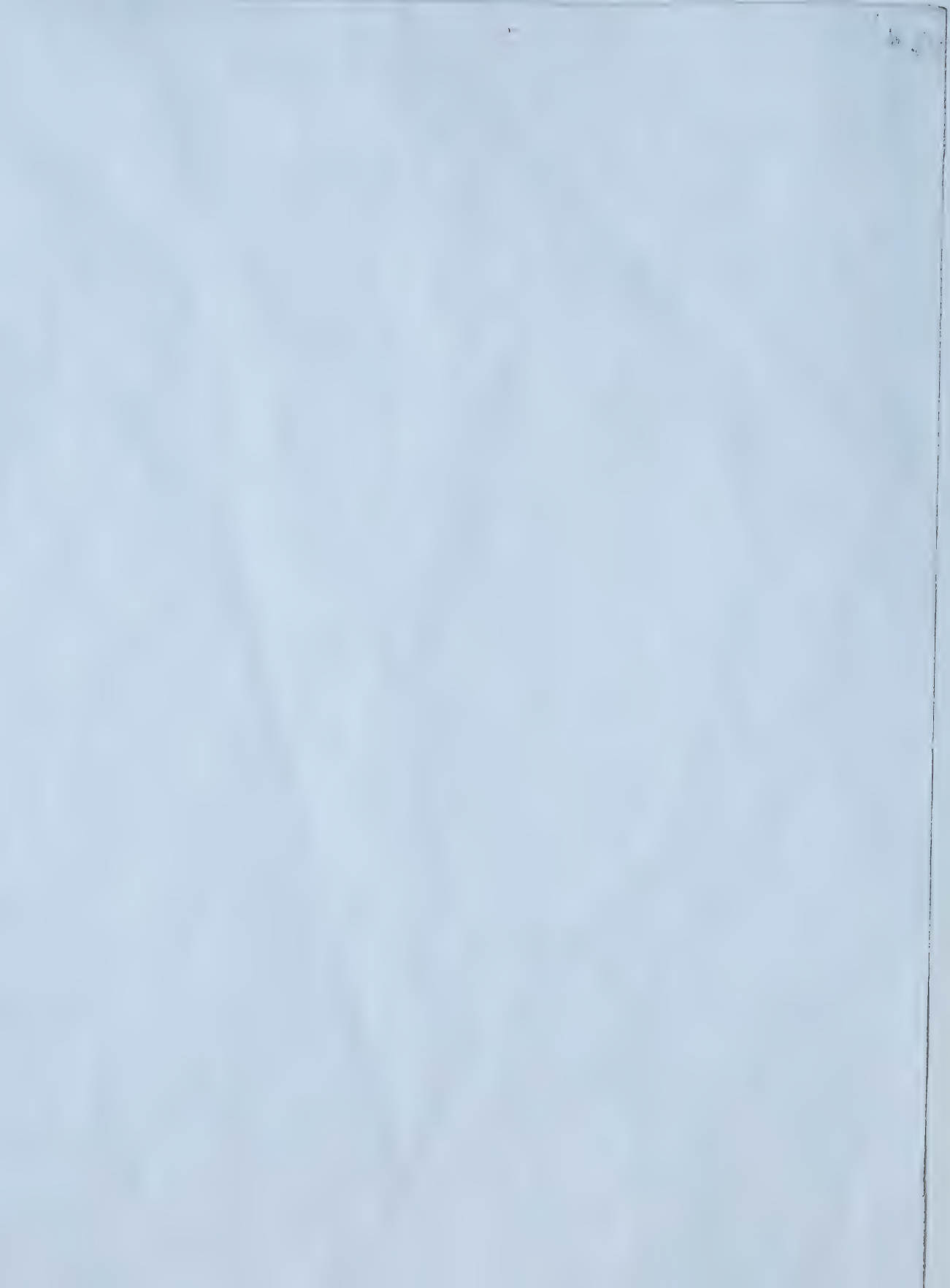
Edmonton, Alberta

Fall 2003

University of Alberta

Faculty of Graduate Studies and Research

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled Synthesis of Naturally Occurring and Synthetic Acetylenes via Alkylidene Carbenoid Rearrangements submitted by Annabelle Liew Kiow Shi Shun in partial fulfillment of the requirements for the degree of Master of Science.



Abstract

Diynes and triynes are common constituents of natural products, many of which exhibit a wide variety of useful biological activities. As a preamble to synthesizing naturally occurring acetylenes, a series of unsymmetrically substituted 1,3-butadiynes and 1,3,5-hexatriynes were made in four steps from commercially available aldehydes or carboxylic acids. The key step involves a Fritsch–Buttenberg–Wiechell rearrangement, whereby an alkylidene carbenoid intermediate rearranges to the desired polyne. This rearrangement occurs under mild conditions, and it is tolerant of a range of functionality. In general, the procedurally facile formation of the dibromoolefinic precursors and the effectiveness of the rearrangement step make this procedure a viable alternative to conventional methods for di- and triyne synthesis. Furthermore, the applicability of this methodology to the synthesis of naturally occurring acetylenes was demonstrated through the total synthesis of three natural products. Finally, a mechanistic investigation into the rearrangement process, via ^{13}C -labelling experiments, was also performed.

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List of Abbreviations

Å	angstrom
α	observed optical rotation in degrees
$[\alpha]^{25}_{\text{D}}$	specific rotation at 25 °C at sodium D line
AlCl ₃	aluminium chloride
Anal.	elemental analysis
anhyd	anhydrous
APT	attached proton test
aq	aqueous
Ar	aryl
<i>t</i> -Bu	<i>tert</i> -butyl
<i>n</i> -BuLi	<i>n</i> -butyllithium
<i>t</i> -BuOK	potassium <i>tert</i> -butoxide
°C	degrees Celsius
ca.	approximately
calcd	calculated
¹³ C NMR	carbon-13 nuclear magnetic resonance
CB ₄	carbon tetrabromide
δ	chemical shift in parts per million
d	doublet
dd	doublet of doublet
dq	doublet of quartet
ε	molar absorptivity
ED	effective dose
ED ₅₀	dose that is effective on 50% of subjects
EI	electron impact
equiv	molar equivalent
ES-MS	electrospray mass spectrometry
Et ₃ N	triethylamine
Et ₂ O	diethyl ether

eV	electronvolt(s)
g	gram(s)
GOESY	gradient Overhauser effect spectroscopy
h	hour(s)
<i>n</i> -hex	<i>n</i> -hexyl
HMBC	heteronuclear multiple bond coherence
HMQC	heteronuclear multiple quantum coherence
¹ H NMR	proton nuclear magnetic resonance
HRMS	high-resolution mass spectrometry
Hz	hertz
<i>i</i> -Pr	isopropyl
IR	infrared
<i>J</i>	coupling constant
K ₂ CO ₃	potassium carbonate
LC	lethal concentration
LC ₅₀	concentration that is lethal to 50% of test subjects
LD	lethal dose
LD ₅₀	dose that is lethal to 50% of test subjects
LDA	lithium diisopropylamide
m	multiplet
M	molar
Me	methyl
MeI	methyl iodide
MeLi/LiBr	methyllithium lithium bromide complex
MeOH	methanol
mg	milligram
MHz	megahertz
mL	millilitre(s)
mmol	millimole(s)
mol	mole(s)

mp	melting point
MS	mass spectrometry
m/z	mass to charge ratio
NaOAc	sodium acetate
NH ₄ Cl	ammonium chloride
nm	nanometer
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
ORTEP	Oak Ridge thermal ellipsoid plot
PCC	pyridinium chlorochromate
Ph	phenyl
PPh ₃	triphenylphosphine
ppm	parts per million
q	quartet
quint	quintet
R_f	retention factor
rt	room temperature
s	singlet
sat.	saturated
SOCl ₂	thionyl chloride
t	triplet
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl
TPA	12- <i>O</i> -tetradecanoylphorbol-13-acetate
TROESY	transverse rotating-frame Overhauser effect spectroscopy
UV	ultraviolet
UV-Vis	ultraviolet-visible

Chapter 1. Introduction

Naturally Occurring Acetylenes

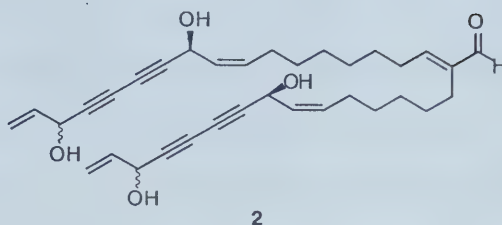
1.1. Introduction

In 1826, the first naturally occurring acetylenic compound, dehydromatricaria ester (**1**), was isolated from an *Artemisia* species.¹ Since then, more than a thousand naturally occurring acetylenes have been reported.² Polyacetylenes, a subset of this class of natural products, have been isolated from a wide variety of plant species,² cultures of higher fungi,^{2a-c,3} bacteria,⁴ and marine sponges.⁵ Polyacetylenes are a unique class of compounds with an interesting array of biological activities, namely antibacterial, antimicrobial, antifungal, antitumor, anticancer, anti-HIV, and insecticidal properties.^{6,7} Extensive reviews on the subject of naturally occurring polyacetylenes have been published over the past 40 years.² We would be remiss were we not to acknowledge the tremendous contribution by Bohlmann in the field of naturally occurring acetylenes, as illustrated by his numerous publications which serve as a reference to everyone.^{2c,e-g} Excellent reviews on the biosynthesis and biological activity of acetylenes have also been written by Bu'Lock,^{2d} Towers,⁷ and Christensen.⁸ The reviews involving acetylenes published by Faulkner in 2002, and earlier, pertained solely to marine natural products.^{5b-d} The most recent review describing the synthesis of polyynes natural products was by Diederich and coworkers in 2000, and dealt only with selected examples of acetylenic coupling reactions.⁹ The limited scope of these recent reports, coupled with intense research efforts still being conducted on naturally occurring acetylenes, led us to assemble a review focusing on, and restricted to, the latest developments in the area of naturally occurring polyynes.



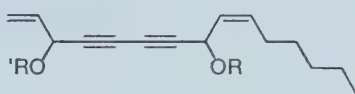
1.2. Diynes

1.2.1. *Aciphylla scott-thomsonii* (Apiaceae)

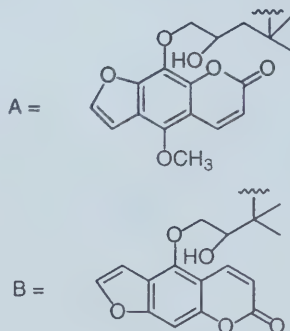


Aciphyllal (**2**) has been isolated from the New Zealand plant *Aciphylla scott-thomsonii*.¹⁰ This C₃₄-polyacetylene is the first reported polyacetylene from a higher plant with a chain length longer than C₁₈. To date, no synthetic preparation has been reported.

1.2.2. *Angelica japonica* (Umbelliferae)



- 3** R = A R' = H
4 R = H R' = A
5 R = B R' = H
6 R = H R' = B



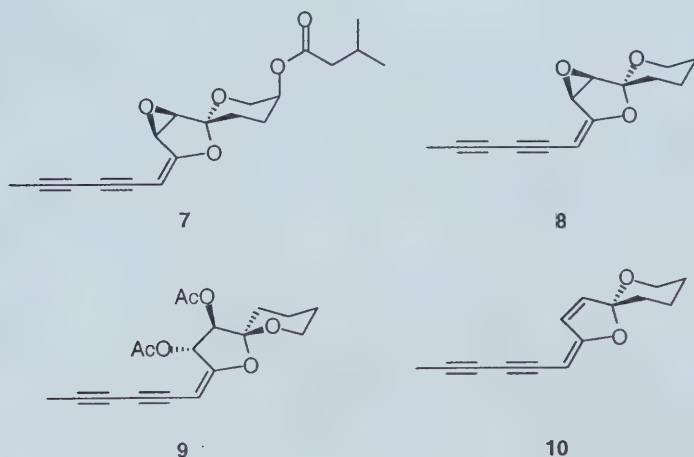
Japoangelols A (**3**), B (**4**), C (**5**), and D (**6**) are antiproliferative furanocoumarin ethers of faltarindiol that have been isolated from the root of *Angelica japonica*.¹¹ Their inhibitory activity against human gastric adenocarcinoma (MK-1) cell growth was investigated, and ED₅₀ values in the range of 7.2–8.5 µg/mL were obtained.¹¹ Neither, however, has been synthesized.

1.2.3. *Artemisia* (Compositae and Asteraceae)

Diacetylenic spiroacetal enol ether derivatives represent an interesting class of compounds. They have been isolated from *Artemisia* plant species, many of which with

reported biological and pharmacological activities.¹² Compound **7**, AL-1, is a specific inhibitor of the activation phase in H₂O₂ production induced by TPA treatment and has been found to have antitumor properties.¹³ Compound **8**, AL-2, also has antitumor properties.¹³ Compound **10** was reported to display antifeedant, antiphlogistic, and spasmolytic activities.^{12c,14,15} Diacetylenic spiroacetal enol ethers **7–10** have a common structural feature: a (2*E*)-(2,4-hexadiynylidene)-1,6-dioxaspiro[4,5]decane framework.^{12d,16} The stereochemical structures of compounds **7** and **8** were elucidated in part by Bohlmann,^{12b} and the stereochemical configuration of the epoxide was solved by Hofer and coworkers.^{16a} Compound **10** was previously synthesized by Bohlmann in 1966 as a mixture of *E*- and *Z*-isomers.¹⁸

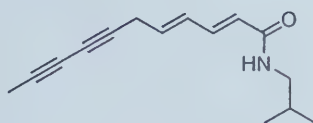
Mukai and Miyakoshi have reported the synthesis of the core framework of the diacetylenic spiroacetal enol ether natural products and thus the first total synthesis of AL-2 (**8**) from diethyl L-tartrate.^{17,18}



1.2.4. *Artemisia dracunculus* (Asteraceae)

Constituents of the aerial parts of *Artemisia dracunculus* included alkamides, pellitorine and a coumarin herniarine.¹⁹ The insecticidal activity of these compounds against rice weevil (*Sitophilus oryzae*) and grain borer (*Rhyzopertha dominica*) was

determined. These two insects are harmful to stocks of corn and barley in Morocco and around the world. Of the compounds tested, acetylenic alkamide **11** showed the strongest insecticidal activity.¹⁹



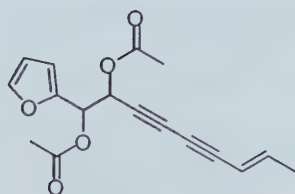
11

1.2.5. *Atractylodes lancea* (Compositae)

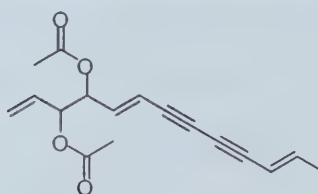
The rhizomes of *Atractylodes lancea* (Thunb.) DC. are used in Chinese traditional medicine to treat rheumatic diseases, digestive disorders, night blindness, and influenza.²⁰ They contain essential oils²¹ and acetylenes such as atractylodin (**12**), atractylodinol (**13**) and acetyl atractylodinol (**14**).²² Recently, a number of new diynes (**15–24**) were identified from the rhizomes of *A. lancea*.²³ Of these compounds, only **24** exhibited strong inhibition of 5-LOX (IC₅₀ 3μM) and COX-1 (IC₅₀ 1μM) activity.^{23b} Atractylodin (**12**) was previously synthesized by Yosioka et al. in 1960, but no yield was reported.²⁴ A novel synthesis of atractylodin (**12**) was achieved by us and will be discussed in detail in Chapter 3 (Scheme 3.4). A key step in the reaction was an alkylidene carbenoid rearrangement.



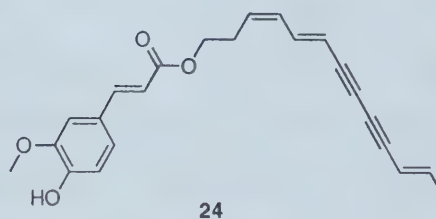
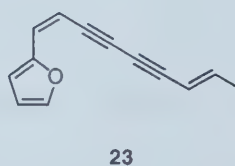
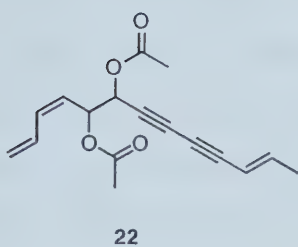
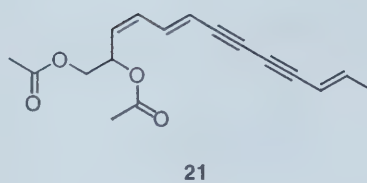
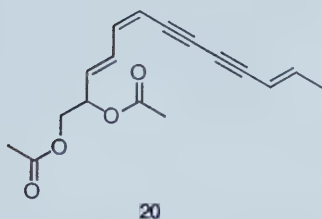
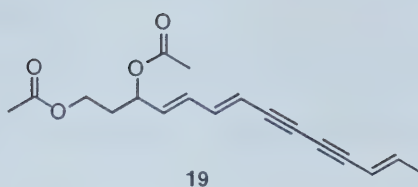
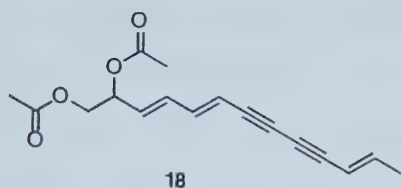
12 R = H
13 R = OH
14 R = OAc



15

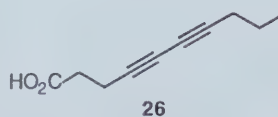
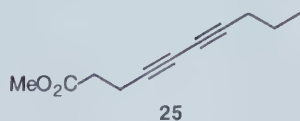


16 erythro
17 threo



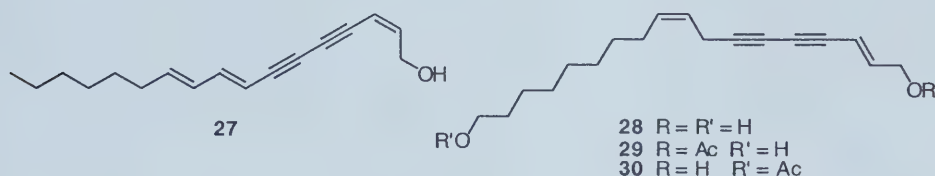
1.2.6. *Bellis perennis* (Asteraceae)

Bellis perennis, the common daisy, is a perennial plant found all across Europe. It is used traditionally to treat rheumatism and as an expectorant.²⁵ In veterinary medicine, it has been utilized as a vulnerary and against ecchymoses. In addition, it has antifungal properties.²⁶ Two novel acetylenes, methyl deca-4,6-dienoate (**25**) and deca-4,6-dienoic acid (**26**), have been isolated from the leaves and flowers of *B. perennis*.²⁷



1.2.7. *Bupleurum acutifolium* (Umbelliferae)

Compounds isolated from the perennial plant *Bupleurum acutifolium* Boiss. include novel acetylenes **27–30**.²⁸ Compounds **28–30** are the first C₁₈-polyacetylenes obtained from the *Bupleurum* genus.

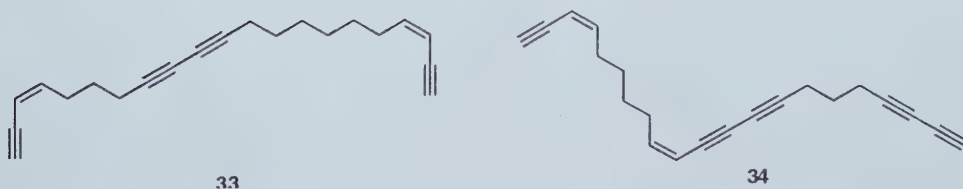


1.2.8. *Callyspongia truncata* (Callyspongiidae)

The Japanese marine sponge *Callyspongia truncata* displayed antifertilization properties against starfish gametes without affecting embryonic cell division.²⁹ Polyacetylene sulfates **31** and **32**, callyspongins A and B, were isolated from *C. truncata* and found to be the metabolites responsible for its fertilization-inhibitory activity.²⁹ Seven additional polyynes, **33–39**, were also isolated from this sponge.³⁰ Compounds **31–39** exhibited significant metamorphosis-inducing activity in the ascidian *Halocynthia roretzi* larvae, with ED₁₀₀ values of 0.13–1.3 µg/mL.³⁰ Callytriols A–E (**35–39**) also displayed antifouling activity against the barnacle *Balanus amphitrite* larvae.³⁰

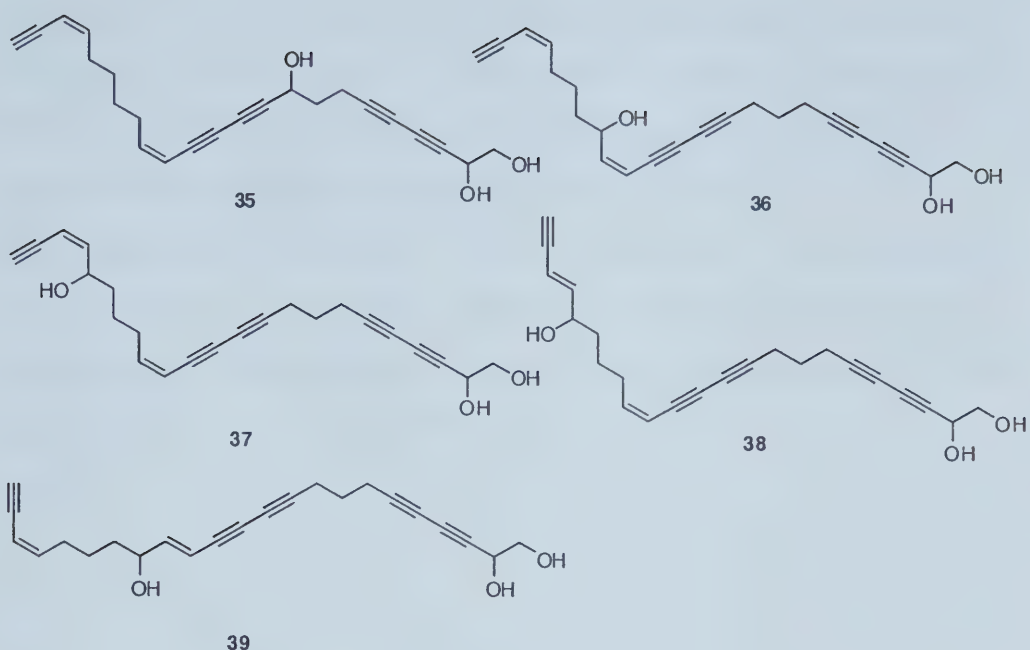


31 R = R' = SO₃Na
32 R = SO₃Na, R' = H



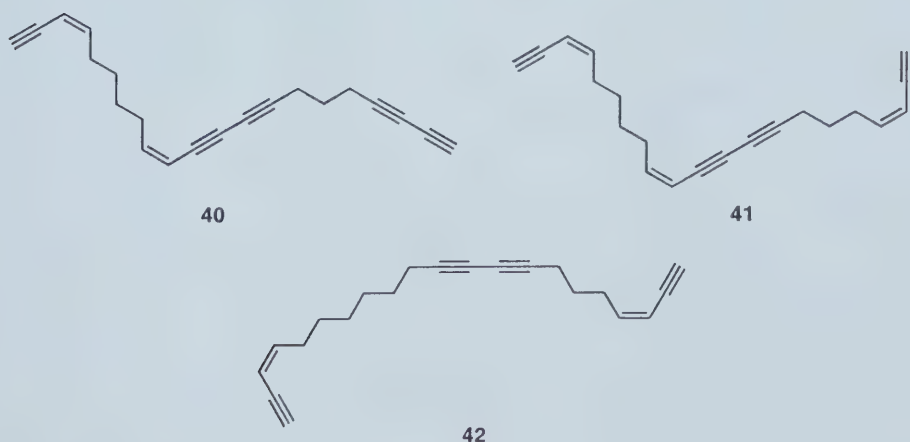
33

34



1.2.9. *Callyspongia* n. sp. (Callyspongiidae)

Callyberynes A–C (**40–42**), having a C_{21} linear chain, were isolated from *Callyspongia* n. sp.³¹



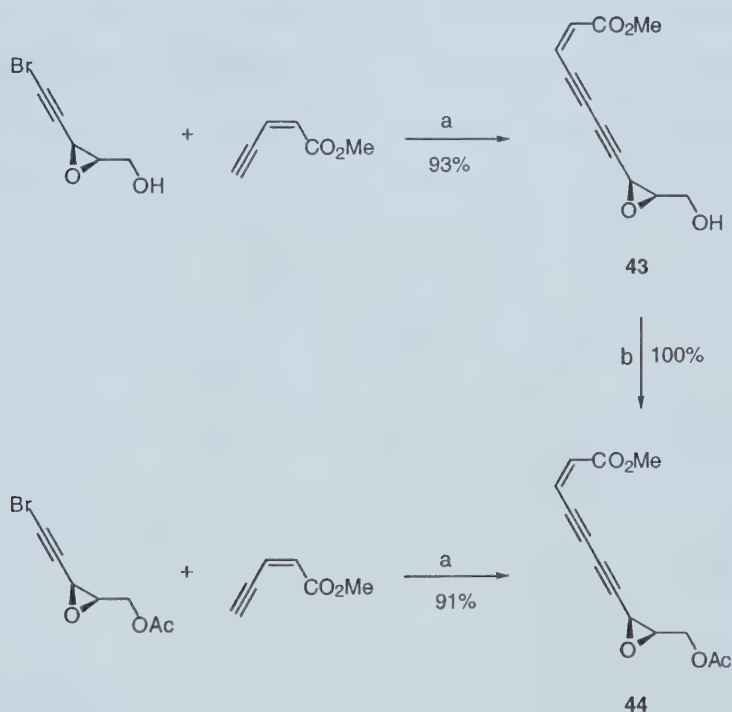
1.2.10. *Chrysothamnus nauseus* and *C. parryi* (Compositae)

Epoxypolyynes have been isolated from higher plants and have been found to exhibit antifungal and insecticidal activities.^{2g,32} Examples of epoxydiynes are compounds **43**

and **44** which were isolated from the Compositae *Chrysothamnus nauseus* and *C. parryi*, and both show antifeedant activity against the Colorado beetle of rabbitbrush.^{32a,b} Pale and coworkers have carried out studies toward asymmetric synthesis of polyene epoxides, and have synthesized compound **43** and its acetate **44**.³³

The synthetic scheme devised by Pale and coworkers involves a Cadiot–Chodkiewicz reaction, using very mild conditions designed to minimize side-reactions such as rearrangement and oxirane opening (Scheme 1.1). This route ultimately afforded **43** in optically pure form in 93% yield and **44** in 91% yield.

Scheme 1.1

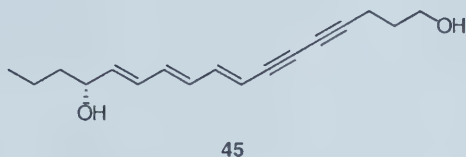


(a) CuCl, NH₂OH•HCl, EtNH₂, MeOH, 0 °C. (b) Ac₂O, DMAP.

1.2.11. *Cicuta virosa* (Umbelliferae)

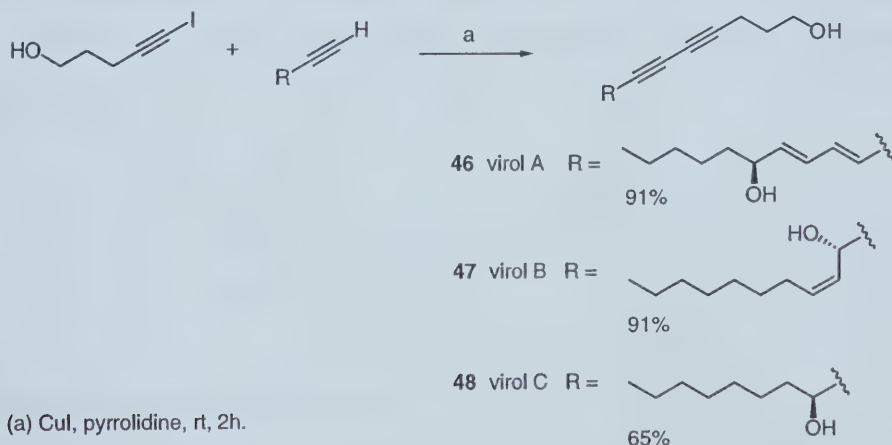
Water hemlock, *Cicuta virosa*, is a well-known toxic plant. The major component is cicutoxin (**45**), a C₁₇-polyacetylene.³⁴ Cicutoxin (**45**) has been found to affect the central

nervous system directly, leading to tonic and clonic convulsions and respiratory paralysis.³⁵ Other diyne constituents of *Cicuta virosa* have recently been isolated.^{36,37b} These include the C₁₇-polyacetylenic analogues, viols A–C (**46–48**), that are chemically more stable than cicutoxin – a factor which enables the study of their mode of pharmacological action.³⁷



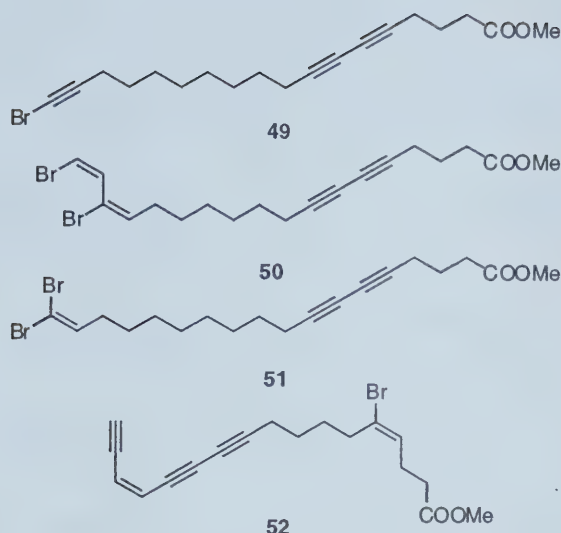
Viols A, B, and C were synthesized by Oshima and coworkers via Cadiot–Chodkiewicz protocols (Scheme 1.2).^{37b} In addition, virol C (**48**) has also been synthesized by Stefani et al. using a chiral sulfoxide for asymmetric induction, and a Cadiot–Chodkiewicz coupling reaction to assemble the diyne core.³⁸

Scheme 1.2



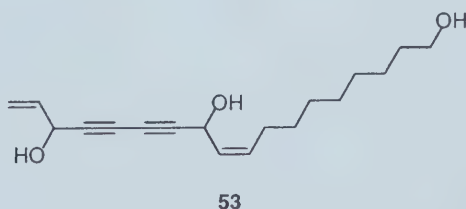
1.2.12. *Cladonia furcata* (Cladoniaceae)

Brominated fatty acids **49–52** were isolated from the lichen *Cladonia furcata* as well as *Lecanora fructulosa*, *Leptogium saturninum*, *Parmelia linctina*, *P. comtseliadalis*, *Peltigera canina*, and *Xanthoria* sp.³⁹



1.2.13. *Cussonia barteri* (Araliaceae)

The C₁₈-polyacetylene **53** was isolated from *Cussonia barteri* (Araliaceae) leaves.⁴⁰ Compound **53** displayed antibacterial activity against *Bacillus subtilis* and *Pseudomonas fluorescens*, antifungal activity against *Cladosporium cucumerinum*, molluscicidal activity against *Biomphalaria glabrata* at low concentrations.⁴⁰ Furthermore, it exhibited hemolytic activity.⁴⁰

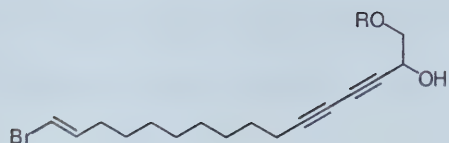


1.2.14. *Diplastrella* sp. (Spirastrellidae)

Novel brominated polyacetylenic diols, diplynes A-E (**54–58**), and sulfated analogues, diplyne A 1-sulfate (**59**), diplyne C 1-sulfate (**60**), and 2-deoxydiplyne D sulfate (**61**), were isolated from the sponge *Diplastrella* sp.⁴¹



54 R = H, R' = Br, R'' = H
 55 R = Br, R' = H, R'' = H
 59 R = H, R' = Br, R'' = SO₃H



56 R = H
 60 R = SO₃H



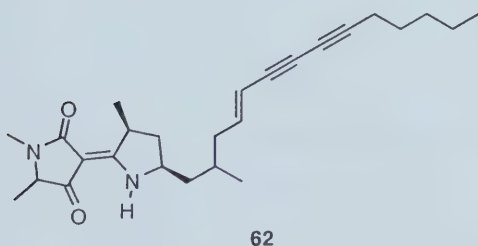
57 R = OH, R' = H
 61 R = H, R' = SO₃H



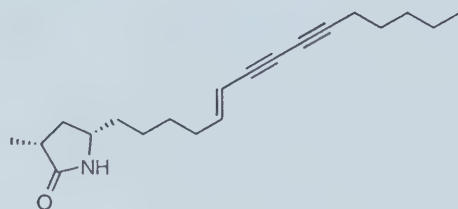
58

1.2.15. *Fischerella muscicola*

Fischerellins A (**62**) and B (**63**) have been isolated from the cyanobacterium *Fischerella muscicola*.^{42,43} Fischerellin A (**62**) is the main anticyanobacterial and algicidal component of *F. muscicola*.⁴² Compound **62** is a strong photosystem-II inhibitor, and **62** also has antifungal and herbicidal properties.⁴² Fischerellin B (**63**) is also an algicidal agent.⁴³



62



63

1.2.16. *Glehnia littoralis* (Apiaceae)

The root of *Glehnia littoralis* F. Schmidt ssp. *Leiocarpa* (Mathias) Hult. (Apiaceae) is used in China and Japan as a diaphoretic, antipyretic, and analgesic drug.⁴⁴ It has also been used by native peoples of North America to treat bladder infections and other ailments.⁴⁴ The antibacterial and antifungal constituents of *G. littoralis* include

Chemical structures of compounds 64 and 65 are shown. Compound 64 is a long-chain molecule with a terminal vinyl group, a terminal hydroxyl group, an internal triple bond, and a 1,2-dihydroxy-3-octyl side chain. Compound 65 is a long-chain molecule with a terminal vinyl group, a terminal hydroxyl group, an internal triple bond, and a 1,2-dihydroxy-3-octyl side chain.

66

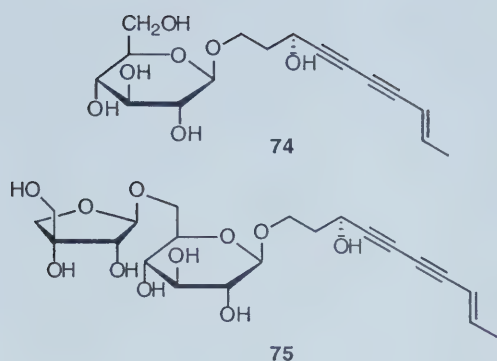
67 R =

69 R =

72 R =

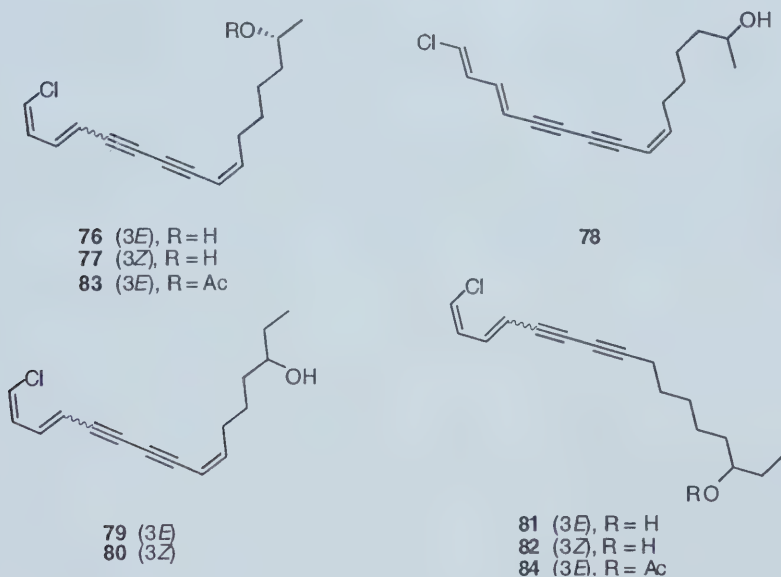
73 R =

68 R = OAc
70 R = H
71 R = OH



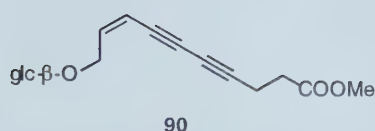
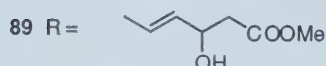
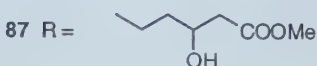
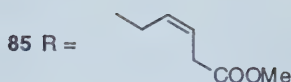
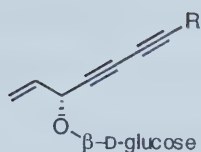
1.2.18. *Haliclona lunisimilis* (Renieridae)

The constituents of the sponge *Haliclona lunisimilis* include six known chlorinated acetylenes (**76–81**), previously isolated from the dorid nudibranch *Diaulula sandiegensis*,⁴⁷ and three new chlorinated acetylenes (**82–84**).⁴⁸



1.2.19. *Helianthus tuberosus* L. (Jerusalem artichoke) (Compositae)

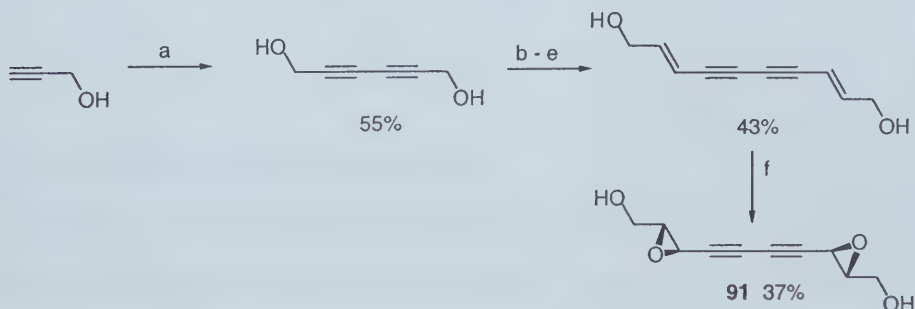
Biologically active constituents of Jerusalem artichoke (*Helianthus tuberosus* L.) included methyl β -D-glucopyranosyl helianthenate A (**85**), B (**86**), C (**87**), D (**88**), E (**89**), and F (**90**).⁴⁹



1.2.20. *Hydnum repandum* (Basidiomycetes)

The symmetrical diyne, repandiol (**91**), a cytotoxic diepoxide, was isolated from the mushrooms *Hydnum repandum* and *Hydnum repandum* var. *album*.⁵⁰ The chemical structure was determined by spectroscopic analysis, and this structure was confirmed by comparison to a synthetic sample of repandiol, efficiently prepared by Nozoe and coworkers (Scheme 1.3).⁵⁰

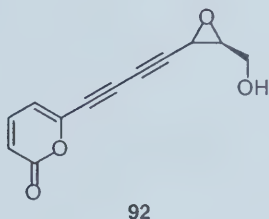
Scheme 1.3



(a) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, CuI , Et_3N , O_2 , DMF , rt. (b) $(\text{COCl})_2$, DMSO , CH_2Cl_2 . (c) Et_3N . (d) $\text{Ph}_3\text{PCHCOOEt}$, -78°C to -20°C . (e) DIBAL , PhH , -78°C . (f) TBHP , $\text{Ti}(\text{O}i\text{Pr})_4$, D-(-)-DET , CH_2Cl_2 , -20°C .

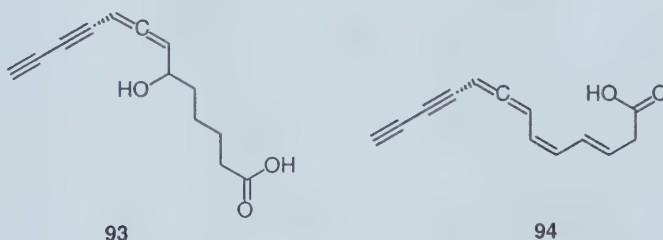
1.2.21. *Junghuhnia nitidu* (Basidiomycetes)

Nitidon (**92**) was isolated from the basidiomycete *Junghuhnia nitidu*.⁵¹ Nitidon showed antibiotic and cytotoxic activities and was found to induce morphological and physiological differentiation of tumor cells at nanomolar concentrations,⁵¹ rendering it an attractive synthetic target.



1.2.22. Fungus LL-07F275

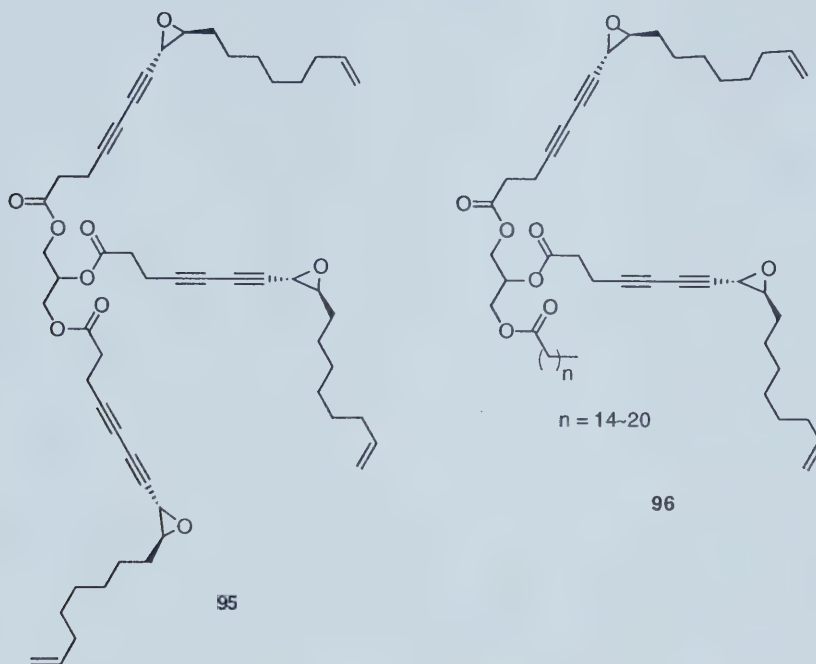
The filamentous, non-sporulating fungus LL-07F275 (NRRL 21081), isolated from a tree bark specimen collected in Panama, was found to be the source of two types of antibiotics. These were diepoxins⁵² and allenic diyne **93**,⁵³ respectively. Compound **93** is structurally related to mycomycin (**94**) on account of their common C₁₃-allenic diynyl functionality.

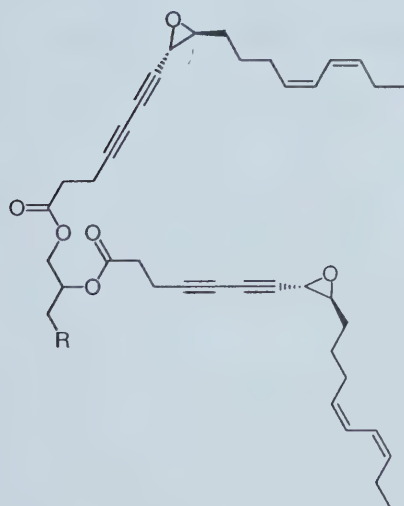
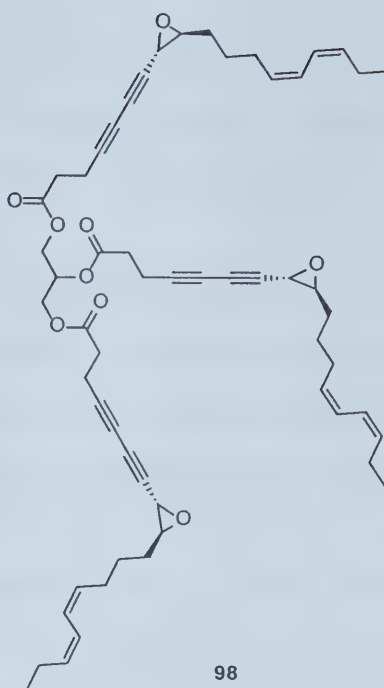
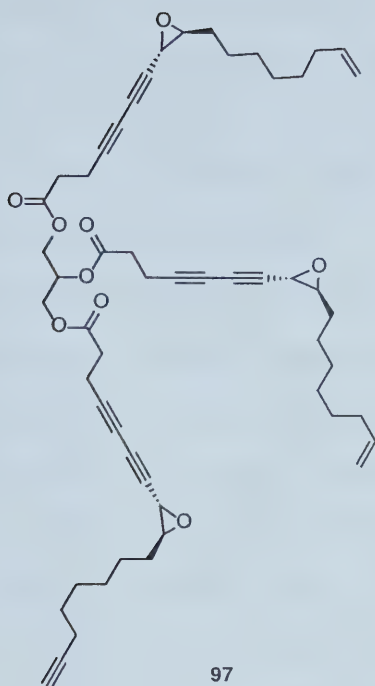


1.2.23. *Lycogata epidendrum* (Myxomycetes)

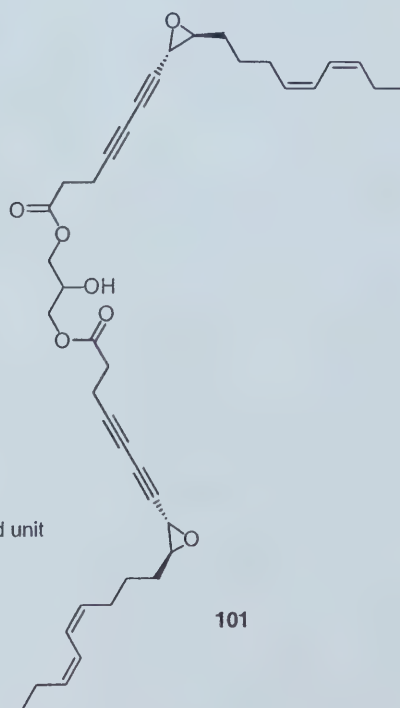
Lycogarides A–G (**95–101**) are structurally quite unusual polyacetylene triglycerides, and have been isolated from the slime mould *Lycogata epidendrum*.⁵⁴ Lycogarides A–C (**95–97**) were found to inhibit completely germination of the root and second coleoptile of rice in husk at 100 ppm.^{54a} The rather complicated core structure of these polyacetylene triglycerides was elucidated by Asakawa and coworkers via 2D-NMR

spectroscopy and chemical degradation.⁵⁴ The stereochemistry of lycogarides A (**95**) and B (**96**) was established by the same authors using the modified Mosher's and dibenzoate exciton chirality methods.^{54a} Similarly, the absolute stereochemistry of lycogaride D (**98**) was determined via the modified Mosher's method.^{54b}





99 R = C₁₆-C₂₀ saturated and unsaturated fatty acid unit
 100 R = OH

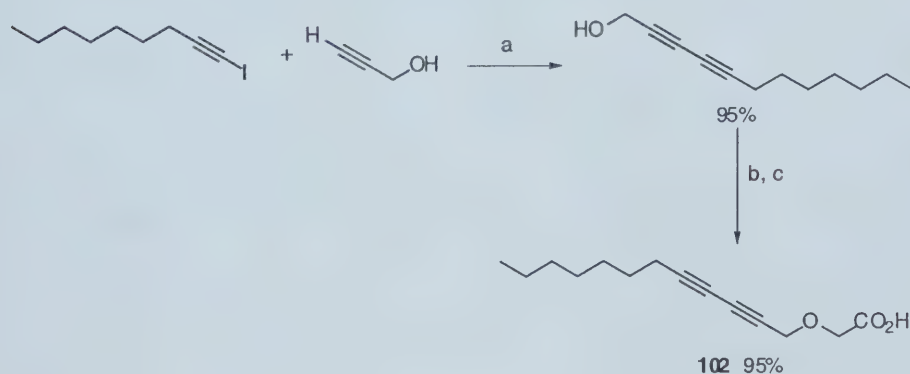


1.2.24. *Montipora* species (Coelentera)

A range of interesting bioactive compounds have been isolated from stony corals,^{55,56,57} including numerous acetylenes.⁵⁸ The genus *Montipora*, in particular, has been a rich source of acetylenic natural products that possess antifungal, antibacterial, ichthyotoxic, and cytotoxic properties.⁵⁸

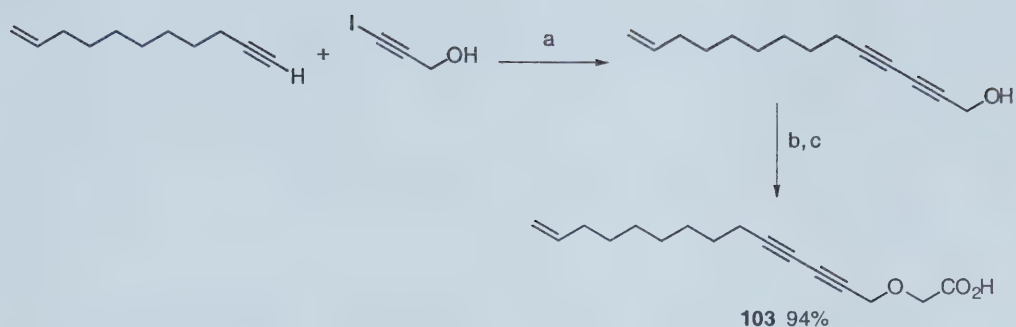
Montipora digitata Dana, 1845 (Scleractinia: Coelenterata) is a hermaphroditic coral. Its colonies liberate bundles of tangled eggs and sperm, and the diene alcohols isolated from the eggs of *M. digitata* have been shown to play a role in the chemotactic activity of the sperm during mass spawning.^{58b} Fusetani et al. examined the bioactive components of the eggs of *M. digitata* and isolated two polyacetylene carboxylic acids, montiporic acids A (**102**) and B (**103**).^{58c} These two compounds displayed antimicrobial activity against *Escherichia coli* and cytotoxicity against P-388 murine leukemia cells.^{58c} Both montiporic acids A and B were synthesized by Stefani, Zeni et al., using Cadiot–Chodkiewicz conditions (Schemes 1.4 and 1.5).⁵⁹

Scheme 1.4



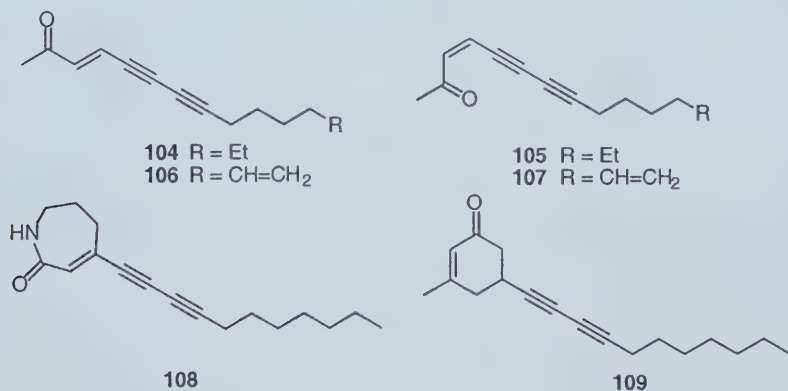
(a) CuI, pyrrrdidine. (b) ethyl 2-bromoacetate, $(n\text{-Bu})_4\text{NHSO}_4$, KOH. (c) HCl.

Scheme 1.5

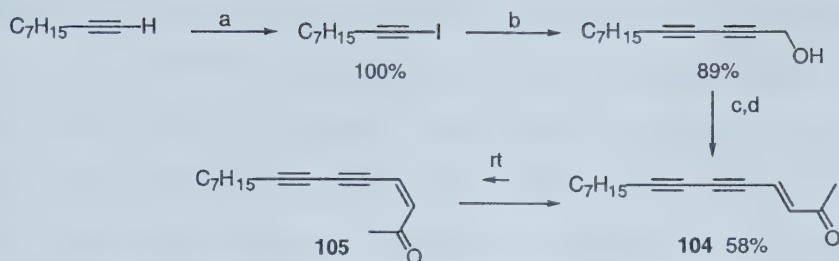


(a) CuI , pyrrolidine. (b) ethyl 2-bromoacetate, $(n\text{-Bu})_4\text{NHSO}_4$, KOH . (c) HCl .

Montiporynes **A–F** (**104–109**) have been isolated from *Montipora* sp. and are reported to exhibit in vitro cytotoxic activity against numerous human solid tumor cell lines.^{58c,d} Thamattoor and Speed have synthesized diacetylenic ketones **104** and **105** in three steps from commercially available starting materials (Scheme 1.6).⁶⁰ Upon standing at room temperature, ketone **104** isomerizes to **105** within hours, leading to an approximate ratio of 3:1 in favor of the *E*-isomer at equilibrium.

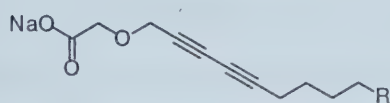


Scheme 1.6



(a) NIS, AgNO₃, acetone. (b) HC≡CH₂OH, pyrrolidine, CuI. (c) (COCl)₂, DMSO, Et₃N. (d) Ph₃P=CHCOCH₃.

Further acetylenes **110–121** were isolated from a brine shrimp fraction of the methanolic extract of *Montipora* sp.⁶¹ These compounds were found to be highly cytotoxic against a series of human solid tumor lines, namely human lung cancer (A549), human ovarian cancer (SK-OV-3), human skin cancer (SK-MEL-2), human CNS cancer (XF498), and human colon cancer (HCT15).⁶¹



110 R = CH=CH₂

111 R = Et

112 R = CH₂CH₂CH=CH₂



113 R = Me

114 R = CH=CH₂



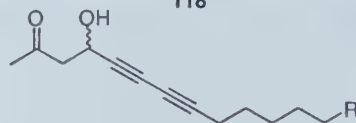
115 R = Et

116 R = CH=CH₂

117 R = CH₂CH₂CH=CH₂



118



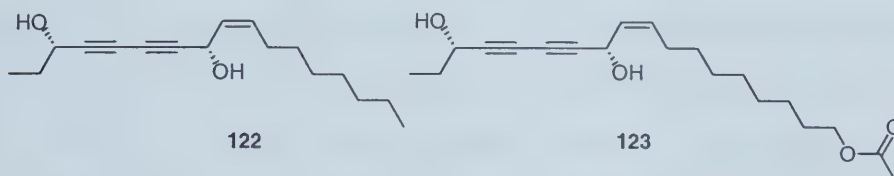
119 R = Et

120 R = CH=CH₂

121 R = CH₂CH₂CH=CH₂

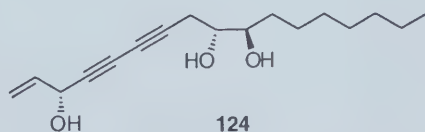
1.2.24. *Oplopanax horridus* (Araliceae)

Oplopanax horridus, commonly known as Devil's Club, is a shrub of western North American forests. First Nations people make use of the inner bark and roots of *O. horridus* to treat diabetes, rheumatism, tuberculosis, colds, headaches, and lung hemorrhages.⁶² Extracts of the inner bark showed antibacterial and antifungal activity,⁶³ as well as activity against *Mycobacterium tuberculosis* and *Mycobacterium avium*.⁶⁴ The polyacetylenes isolated from *O. horridus* displayed antimycobacterial and antifungal activity.⁶⁵ Of these acetylenes, **122** and **123** were novel compounds.⁶⁵



1.2.25. *Panax ginseng* (Araliceae)

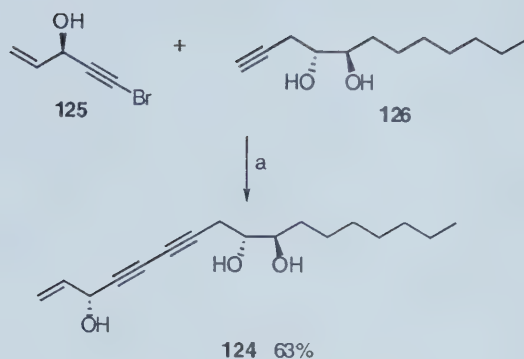
Red ginseng, the steamed and dried root of *Panax ginseng* C. A. Meyer, has been used extensively in oriental traditional medicine as an analeptic, erythropoietic, and stomachic agent.⁶⁶ Panaxytriol (**124**), isolated in 1983, is believed to be a major constituent responsible for the biological activity of red ginseng.⁶⁷ Panaxytriol has been found to inhibit MK-1 cells ($IC_{50} = 8.5$ ng/mL) and to suppress the growth of B16 melanoma cells transplanted into mice.⁶⁸ In addition, its effectiveness at inhibiting cellular respiration and energy balance of a human breast carcinoma cell line has been reported.⁶⁹ It was also found to increase the cytotoxicity of mitomycin C against human gastric adenocarcinoma cell lines.⁷⁰



The chemical structure of panaxytriol was elucidated in 1987.⁷¹ In 1995, Kobayashi et al. proposed the absolute configuration of panaxytriol to be (3*R*,9*R*,10*R*), using the modified Mosher ester and the dibenzoate CD exciton chirality methods.⁷² Since this initial report, however, the issue of the relative and absolute stereochemistry of panaxytriol has been a matter of controversy due to conflicting data.^{73–77} In 1997, Fujimoto and coworkers proposed a different absolute configuration: (3*R*,9*S*,10*S*),⁷³ based on the synthesis of panaxytriol derivatives and a comparison of optical rotations and NMR spectra with corresponding derivatives of panaxytriol from natural sources. Shortly thereafter, Kobayashi disputed Fujimoto's findings on the basis of Hudson's rule, and repropounded the configuration (3*R*,9*R*,10*R*).⁷⁴ In 1999, Cai and coworkers synthesized the (3*R*,9*R*,10*R*) and (3*R*,9*S*,10*S*) diastereomers of panaxytriol and, by comparing the optical rotations of the diastereomers and natural panaxytriol, they concluded that the absolute configuration of the natural product was (3*R*,9*R*,10*R*).^{75,76} However, Gurjar et al. came to a different conclusion and were proponents of the (3*R*,9*S*,10*S*) configuration.⁷⁷ Gurjar et al. synthesized four diastereomers of panaxytriol and compared the optical rotations of these diastereomers and their acetonide derivatives with the natural compound and its derivative.

The ongoing debate about the stereochemistry of panaxytriol elicited further enantioselective syntheses. In the past year, three independent syntheses of panaxytriol **124** have been reported.^{78–80} Interestingly, all three are in favor of the (3*R*,9*R*,10*R*) configuration. The most recent synthesis of panaxytriol has been accomplished by Danishefsky and Yun.⁷⁸

Scheme 1.7



(a) CuCl , EtNH_2 , $\text{NH}_2\text{OH}\cdot\text{HCl}$, MeOH , 0°C , 1 h.

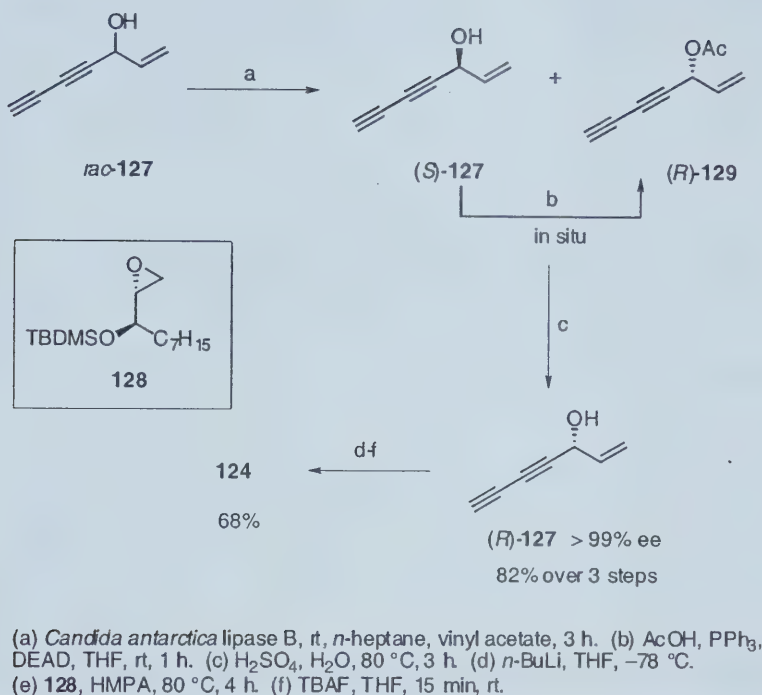
One of the objectives of Danishefsky and Yun was to establish the stereochemistry of panaxytriol rigorously through chemical synthesis. In this quest, the precursors for the Cadiot–Chodkiewicz cross-coupling reaction were synthesized enantioselectively, and their stereochemistry was established by Mosher ester methodology. A key step in the enantioselective synthesis of panaxytriol by Danishefsky and Yun is an innovative Cadiot–Chodkiewicz cross-coupling which portrays the applicability of this coupling reaction to a setting of three unprotected hydroxyl groups (Scheme 1.7). Finally, the optical rotation of the synthetic (3*R*,9*R*,10*R*) panaxytriol was compared to that of the authentic natural product and they were found to be consistent, thus leading the authors to assign the configuration of natural panaxytriol as (3*R*,9*R*,10*R*).

Faber and coworkers used an alternative route for the synthesis of panaxytriol (8% overall yield).⁷⁹ Their synthetic strategy involved two main building blocks: alcohol (*R*)-**127** and epoxy-alcohol (2*R*,3*R*)-**128**.

The alcohol **127** was first prepared in racemic form from 1,4-dichlorobutyne and acrolein, and (*R*)-**127** was then obtained enantioselectively by *Candida antarctica* lipase B-catalyzed kinetic resolution via acyl-transfer (Scheme 1.8). This kinetic resolution process was associated with an in situ inversion which thus prevented the occurrence of

the undesired isomer. As a result, (*R*)-**127** was isolated in >98% ee from the racemate in 82% yield.

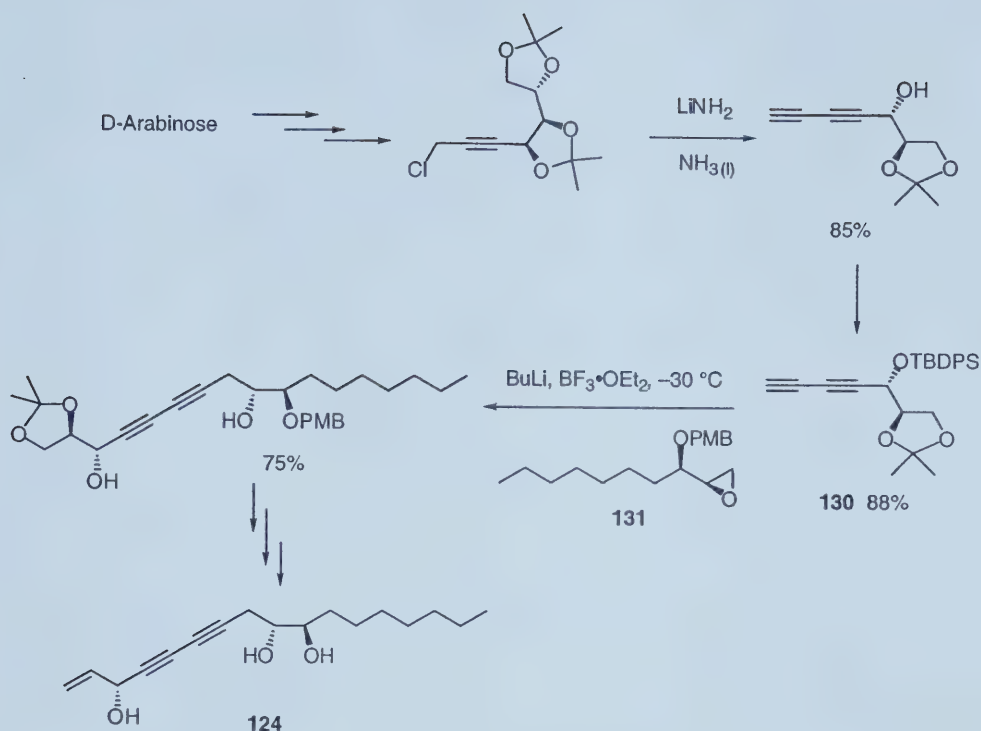
Scheme 1.8



Condensation of diyne (*R*)-**127** with optically pure **128** gave (3*R*,9*R*,10*R*) panaxytriol. The authors mentioned that the optical rotation of the synthetic product agreed with the reported values for naturally occurring panaxytriol. Parenthetically, Faber and coworkers also carried out the synthesis of the (3*S*,9*R*,10*R*) isomer of panaxytriol and both enantiomers of falcarinol by related methods.

Yadav et al. have synthesized (3*R*,9*R*,10*R*) panaxytriol from D-arabinose using base induced double elimination of 4,5-*O*-isopropylidene propargyl chloride as a key step to introduce the diyne moiety (Scheme 1.9).⁸⁰ As with Faber's synthesis, panaxytriol (**124**) was elaborated via conversion of terminal diyne **130** into its acetylide derivative followed by a condensation reaction with epoxide **131** under Yamaguchi conditions.

Scheme 1.9



Ginsenoyne L, M, and N (**132–134**) constitute an interesting series of diynes isolated from the root of *Panax ginseng*.⁸¹ Biogenetic consideration of compounds **132** and **133** suggests that they are Diels–Alder type adducts derived from caryophyllene and ginsenoyne **135** (Figure 1.1). Similarly, compound **134** appears to be derived from bicyclogermacrene and **135**.

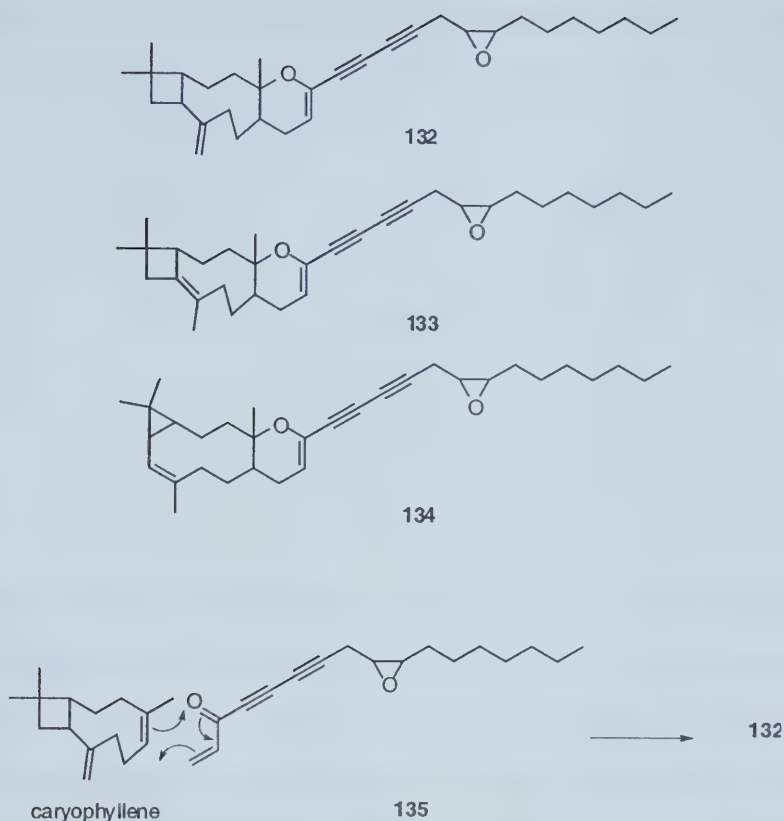
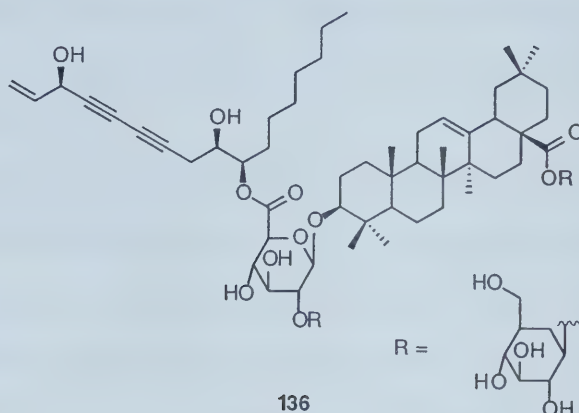


Figure 1.1. Diels-Alder type reaction between caryophyllene and 135.

In 2001, polyacetyleneginsenoside-Ro **136**, a novel compound, was isolated from the root of *Panax ginseng* C. A. Meyer.⁸² Diyne **136** is comprised of two substructures: an oleanolic acid-derived triterpene saponin and a butadiyne unit, both of which have previously been isolated from *Panax ginseng* as separate compounds. Polyacetyleneginsenoside-Ro was determined to inhibit the replication of HIV-1 (IC_{50} = 13.4 $\mu\text{g/mL}$). It was nontoxic toward the cultured cells up to a concentration of 20 $\mu\text{g/mL}$. The authors have postulated that, considering the reported role of the monoterpene components of *Gleditsia* and *Gymnocladus* saponins in the modulation of the anti-HIV activities of these compounds, the diyne unit of **136** might be responsible

for the enhanced antiviral characteristics of **136** in comparison with the other published HIV-1 inhibitory saponins.



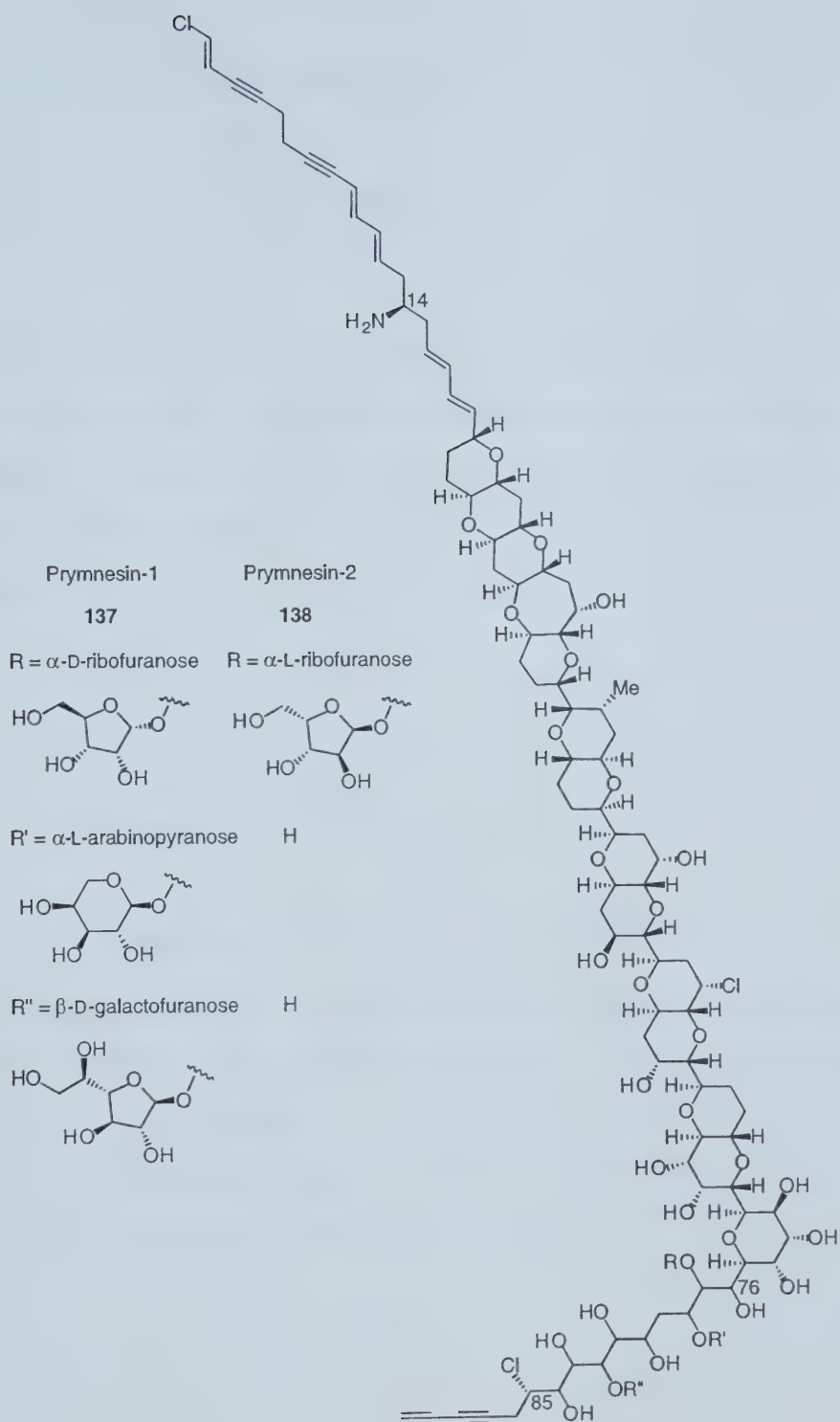
It is worth noting that the authors have assigned the stereochemistry of polyacetyleneginsenoside-Ro based on the findings of Gurjar et al. concerning the stereochemistry of naturally occurring panaxytriol.⁷⁷ Considering that subsequent syntheses of panaxytriol have demonstrated that the stereochemistry of naturally occurring panaxytriol is (3*R*,9*R*,10*R*),^{78–80} this suggests that further investigation into the stereochemical assignment of polyacetyleneginsenoside-Ro may be desirable. To date, however, **136** has not been synthesized.

1.2.25. *Prymnesium parvum* (Haptophyceae)

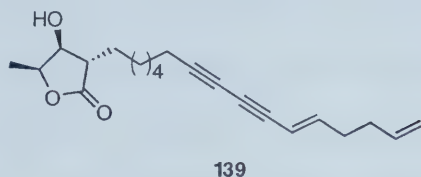
The red tide phytoflagellate *Prymnesium parvum* is extremely harmful to coastal ecology worldwide, and is a significant threat to fish farming, particularly in low-salinity water.⁸³ Since 1961, this microalgal organism has been known to produce a potent hemolytic and ichthyotoxic agent, prymnesin.⁸⁴ However, because of extreme difficulty in isolation along with the high structural complexity of the toxin, its chemical structure has been the subject of speculation for over 30 years.⁸⁵ Upon optimizing culture conditions, Yasumoto and coworkers achieved a 20-fold increase of prymnesins, and isolated prymnesin-1 (**137**) and prymnesin-2 (**138**).⁸⁶ Compounds **137** and **138** were

found to be potent hemolytic and ichthyotoxic agents.^{86,87} The planar structure of prymnesin-2 (**138**) was reported by Yasumoto and coworkers in 1996.⁸⁸ Shortly thereafter, the relative stereochemistry of prymnesin-2 (**138**) and the structure of prymnesin-1 (**137**) were elucidated by the same authors, by using NMR and chiral GC analytical techniques.⁸⁹

Prymnesin-2 (**138**) has the molecular structure $C_{96}H_{136}Cl_3NO_{35}$. This compound has the following unique structural attributes: a C_{90} unbranched carbon chain (with the exception of a methyl group), five contiguous ether rings (6/6/6/7/6), four 1,6-dioxadecalin moieties, conjugated double and triple bonds, chlorine and nitrogen atoms, and an uncommon L-xylose. Prymnesin-1 (**137**) has the molecular structure $C_{107}H_{154}Cl_3NO_{44}$, and possesses the same aglycone structure as prymnesin-2 along with α -D-ribofuranosyl, α -L-arabinosyl, and β -D-galactofuranosyl residues at C77, C78 and C82 positions, respectively. In the polycyclic parts (C20–C74) of both toxins, all ring fusions were *trans* and all rings had a chair conformation. C14 and C85 have recently been determined to have (*S*)-configuration.⁹⁰ The stereochemistry at C76–C84 has not yet been elucidated.

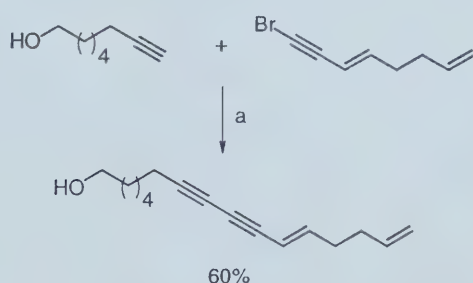


1.2.26. *Sapranthus palanga* (Annonaceae)



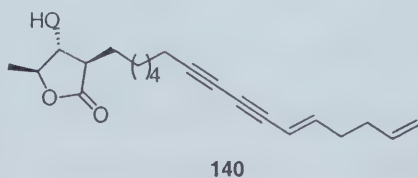
(-)-Sapranthin was isolated from the bark of *Sapranthus palanga* in 1986 with the proposed structure **139**.⁹¹ Diyne **139** was subsequently synthesized by Brückner and coworkers.⁹² A key step is a Cadiot–Chodkiewicz reaction using conditions developed by Vasella and Cai⁹³ (Scheme 1.10).

Scheme 1.10



(a) Pd(**dba**)₂, CuI, LiI, DMSO, rt, 10 min; pentamethylpiperidine, 2h.

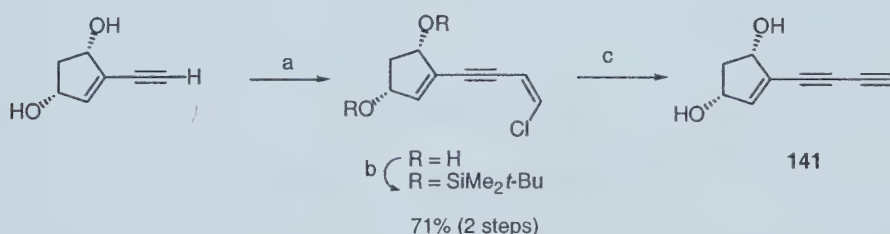
Interestingly, comparison of the NMR data of the synthetic sample of compound **139** with that of the authentic sapranthin revealed discrepancies. The authors deduced that the true structure of natural sapranthin was in fact that of **140**, a diastereomer of **139**. This premise was confirmed synthetically: the NMR spectral data and optical rotation of synthetic **140** matched that of the natural sapranthin sample.



1.2.27. *Sistorema raduloides* (Corticaceae: Basidiomycotina)

Sistodiolynne (**141**), a polyketide metabolite of the wood rot decay fungus *Sistorema raduloides*,⁹⁴ was first isolated by Ayer and coworkers and its stereochemistry was established via circular dichroism methods. Sistodiolynne has been synthesized by Sugahara and Ogasawara.⁹⁵ They constructed the 1,3-butadiyne unit of sistodiolynne using a coupling reaction developed by Kende and Smith (Scheme 1.11).⁹⁶ Sistodiolynne could not be isolated pure on account of its inherent instability and propensity to polymerize even in solution. However, its ¹H NMR data coincided with that of the natural product, thus confirming the structure of naturally occurring sistodiolynne.⁹⁵

Scheme 1.11



(a) (Z)-ClHC=CHCl, Pd(PPh₃)₄, CuI, BuNH₂, PhH, 0.5 h. (b) *t*-BuMe₂SiCl, imidazole, DMF.
(c) Bu₄NF, THF, rt, 10 h.

1.2.28. *Strongylophora* (Petrosiidae)

Strongylodiols A–C (Figure 1.2) constitute a novel class of cytotoxic long-chain acetylenic alcohols which have been isolated from an Okinawan marine sponge of the genus *Strongylophora*.⁹⁷ Strongylodiols A–C display potent cytotoxic activity against human T lymphocyte leukemia (MOLT-4) cells.⁹⁷ Upon determination of their stereochemical configuration at C6, using the modified Mosher's method, Iguchi and coworkers found that these acetylenic alcohols occurred as an enantiomeric mixture with a different ratio: 91:9 for strongylodiol A, 97:3 for strongylodiol B, and 84:16 for

strongylodiol C.⁹⁷ The major enantiomer in all three cases had the *R* configuration, as established by the modified Mosher's method. Moreover, each enantiomer was separated and characterized fully. The only member of this class to be synthesized is (*R*)-strongylodiol A (**142**), and the synthesis was carried out by Yadav et al.⁹⁸ The key step in the synthetic scheme involves enantioselective synthesis of intermediate **149** by β -elimination of epoxychloride **148** (Scheme 1.12), followed by a Cadiot–Chodkiewicz cross-coupling reaction between **149** and 3-bromo-2-propyne-1-ol.

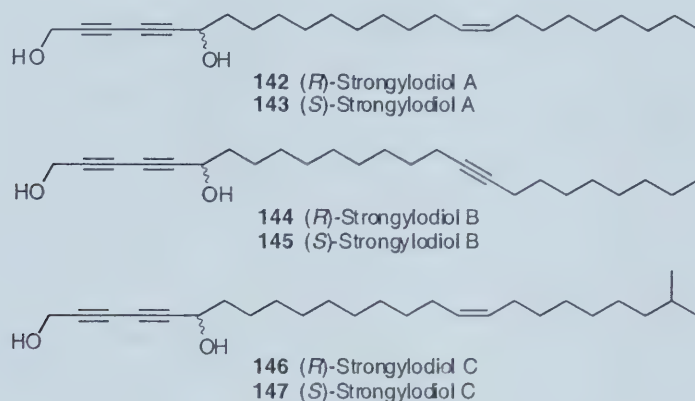
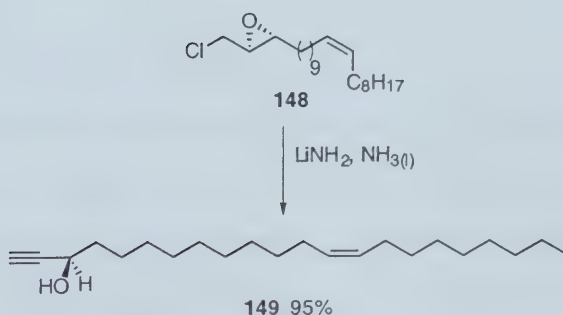


Figure 1.2. Strongylodiols A–C

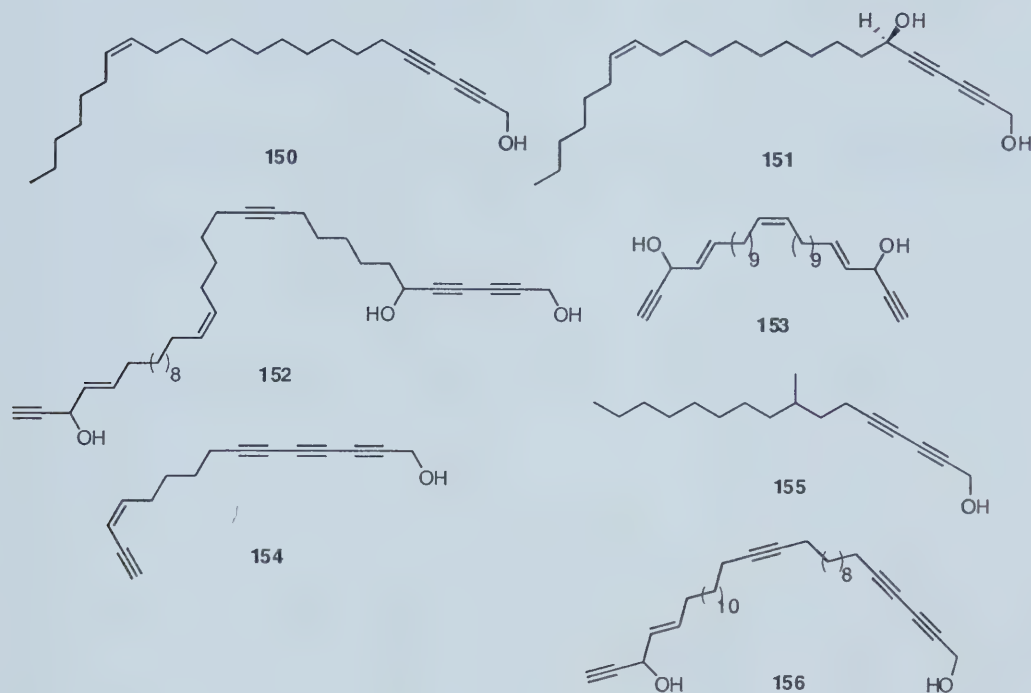
Scheme 1.12



1.2.29. *Strongylophora durissima* (Petrosiidae)

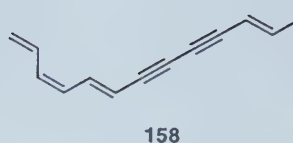
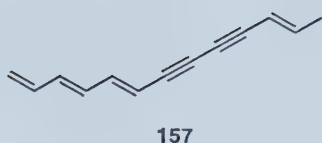
The crude extract of the marine sponge *Strongylophora durissima* has been found to display strong ichthyotoxicity.⁹⁹ The acetylenes isolated from *S. durissima* include

renierin-2 (**150**),¹⁰⁰ 18-hydroxyrenierin-2 (**151**),¹⁰⁰ melyne-C (**152**),¹⁰¹ duryne (**153**),¹⁰² and siphanochalynol (**154**).¹⁰³ Recently, two new polyynes, durissimols A (**155**) and B (**156**) were identified.¹⁰⁴ Of these aforementioned acetylenes, durissimol B (**156**) and duryne (**153**) exhibited significant cytotoxicity against human gastric tumor (NUGC) cells.¹⁰⁴

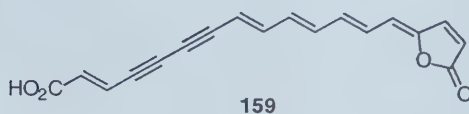


1.2.30. *Viguiera annua* (Asteraceae)

Polyynes **157** and **158** were isolated from the leaves of *Viguiera annua*.¹⁰⁵ Despite the fact that the compounds **157** and **158** showed phototoxicity toward insects, the larvae of *Zygogramma continua* Le Conte (Coleoptera: Chrysomelidae) were able to feed on the leaves of *V. annua*.¹⁰⁵ The tolerance of this insect to the insecticidal acetylenes might be due to light-avoidance behavior and the inducibility of certain antioxidant enzymes in *Z. continua* larvae.¹⁰⁵

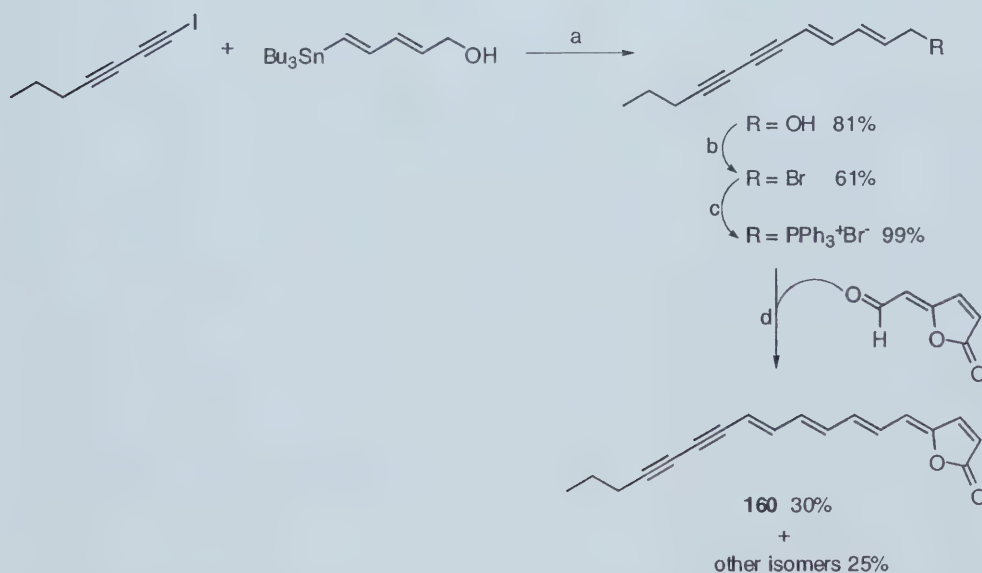


1.2.31. *Xerula melanotricha* Dörfelt (Tricholomataceae)



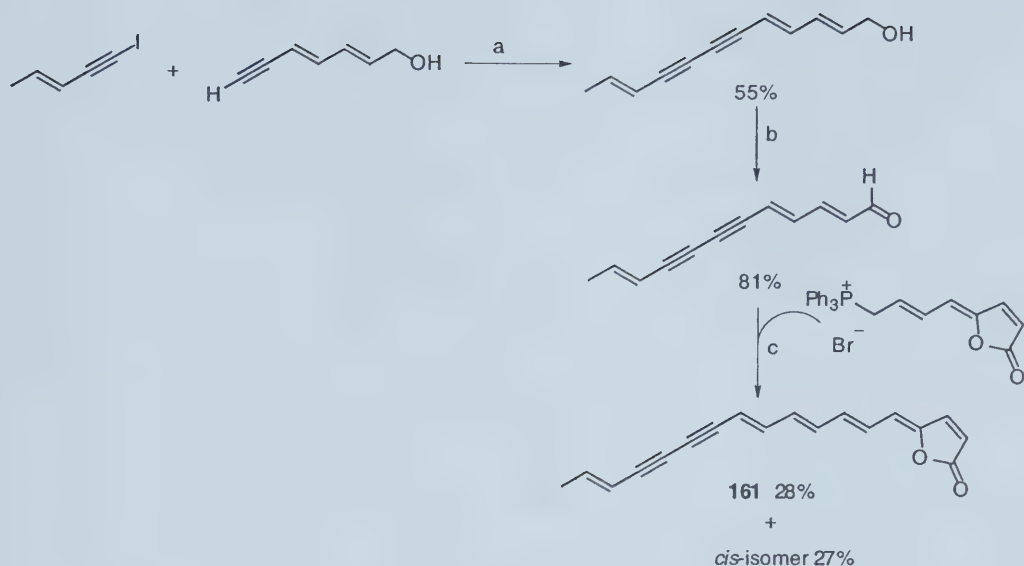
Three unique γ -alkyldenebutenolides, xerulinic acid (**159**), dihydroxyxerulin (**160**), and xerulin (**161**), were isolated from *Xerula melanotricha* Dörfelt.¹⁰⁶ Xerulin and dihydroxyxerulin, obtained as inseparable 90:10 – 65:35 mixtures, inhibited the biosynthesis of cholesterol in HeLa S3 cells (ID₅₀ 1 μ g/g) without any cytotoxicity.¹⁰⁶ Dihydroxyxerulin and xerulin have been synthesized by Siegel and Brückner (Schemes 1.13 and 1.14).¹⁰⁷

Scheme 1.13



(a) LiCl, PdCl₂(PPh₃)₂, THF, rt, 5h. (b) NaBr, BF₃•OEt₂, MeCN, rt, 6h. (c) PPh₃, MeCN, rt, 12h. (d) *n*-BuLi, THF, -83 °C – rt.

Scheme 1.14



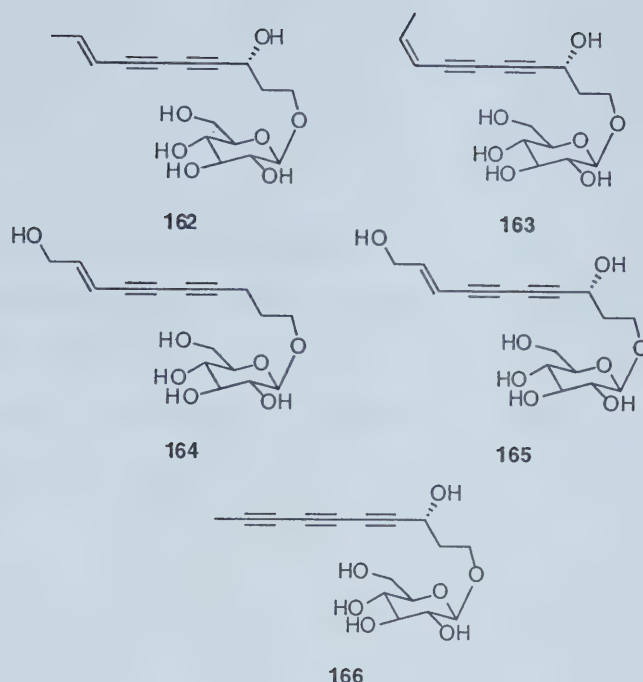
(a) $\text{Pd}(\text{dba})_2$, CuI , $\text{THF}/i\text{-Pr}_2\text{NH}$, rt, 15 min. (b) Dess-Martin periodinane, CH_2Cl_2 , rt, 5 min. (c) K_2CO_3 , CH_2Cl_2 , 90°C .

1.3. Triynes

1.3.1. *Bidens parviflora* WILLD. (Compositae)

The plant *Bidens parviflora* WILLD. is used in traditional Chinese medicine as an antipyretic, anti-inflammatory, and antirheumatic agent.¹⁰⁸ In addition to four novel diyne glucosides, **162–165**, triyne **166** has been isolated from *B. parviflora*.¹⁰⁹

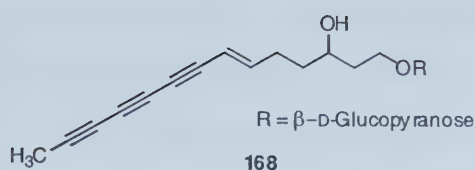
The inhibitory activity of compounds **162–166** on histamine release from rat peritoneal exudates cells induced by antigen–antibody reaction was studied and they were found to have a much higher inhibitory effect ($\text{IC}_{50} = 0.072\text{--}0.186\ \mu\text{M}$) than the potent anti-inflammatory agent, indomethacin ($\text{IC}_{50} = 0.625\ \mu\text{M}$).¹⁰⁹



1.3.2. *Bidens pilosa* L. (Asteraceae)

The leaves and flowers of *Bidens pilosa* L. have been used in Mexican traditional medicine as treatment for stomach disorders, hemorrhoids, and diabetes.¹¹⁰ *B. pilosa* is also an antimicrobial compound due to its antibiotic component phenylhepta-1,3,5-triyn (167).¹¹¹ Furthermore, *B. pilosa* has demonstrated cocarcinogenic activity for papilloma induction in rat esophagus.¹¹² Other constituents of this plant include lipophilic acetylenes,¹¹¹ phenylpropanoids,¹¹³ and chalcone and aurone glucosides.^{113,114} Recently, novel acetylenes 168 and 169 have been isolated.^{110,115} Compound 168 exhibited overgrowing action against normal and transformed human cell lines in culture.¹¹² A novel synthesis of triyne 167 was accomplished via an alkylidene carbenoid rearrangement by us and will be discussed in Chapter 3.





1.3.3. *Callyspongia* sp. (Callyspongiidae)

A series of polyacetylenes were isolated from the Red Sea sponge *Callyspongia* sp. and these include aikupikanynes A (**170**), B, C, D, E (**171**), and F (**172**),¹¹⁶ and callyspongenols A–C (**173–175**).¹¹⁷ Compounds **173–175** exhibited moderate cytotoxicity against P388 and HeLa cells.¹¹⁷



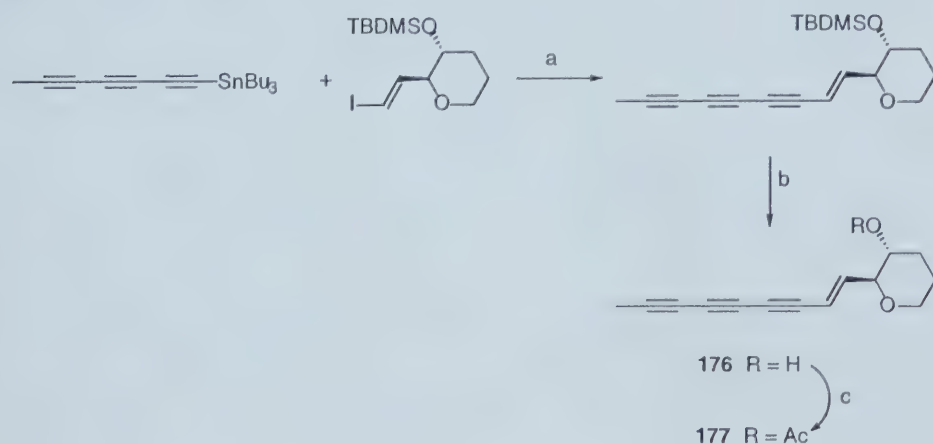
1.3.4. *Dahlia coccinea* (Compositae) and *Ichthyother terminals* (Compositae)

In 1965, (–)-ichthyothereol **176** and its acetate **177** were isolated from the plants *Dahlia coccinea* and *Ichthyother terminals*.¹¹⁸ The latter has been known to natives of the Lower Amazon Basin as a fish poison,^{118,119} and it has also been found to be poisonous to mammals.¹¹⁸ Ichthyothereol and its acetate were shown to be highly toxic

to the fish *Lebistes reticulatus*, thus substantiating their contribution to the toxicity of *Ichthyother terminals*.^{118,119} Compounds **176** and **177** were also found to be toxic to mice.¹¹⁸ Tentative assignment of the stereochemistry was made by Jones, Durham and coworkers in 1965 based on ¹H NMR analysis^{118,119} and on the optical rotatory dispersion curve of the substituted tetrahydropyran-3-one derivatives made by oxidation of perhydroichthyothereol.¹¹⁸ The absolute configuration of **176** and **177** was confirmed by Jones and coworkers in 1970 via chemical transformation of **176** into the (–)-bis(2,4-dinitrobenzoate) of *trans*-3-hydroxymethyltetrahydropyran.¹²⁰ Surprisingly, it was not until 2001 that the total synthesis of ichthyothereol and its acetate were published by Mukai et al.¹²¹

Mukai's synthesis relies on Tykwinski's carbenoid rearrangement to assemble the triyne core, followed by a Stille coupling reaction to complete the core structure (Scheme 1.15).¹²⁰

Scheme 1.15

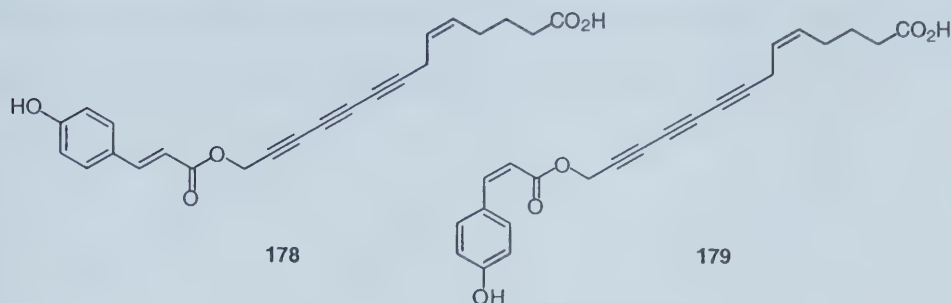


(a) 5 mol % PdCl₂(PPh₃)₂, rt. (b) TBAF, THF, rt. (c) Ac₂O, DMAP, CH₂Cl₂, rt.

1.3.5. *Fistula hepatica* (Basidiomycetes)

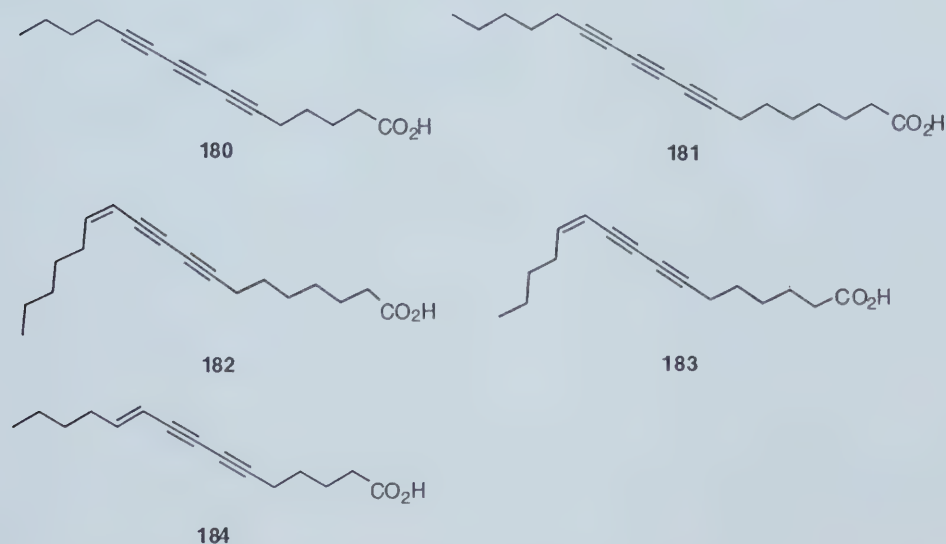
Cinnatriacetins A (**178**) and B (**179**) were isolated from the fruiting bodies of the Japanese edible mushroom *Fistula hepatica*.¹²² Compounds **178** and **179** were active

against Gram-positive bacteria, but they were inactive against Gram-negative bacteria, yeast and other fungi. The synthesis of neither isomeric natural product has been reported.



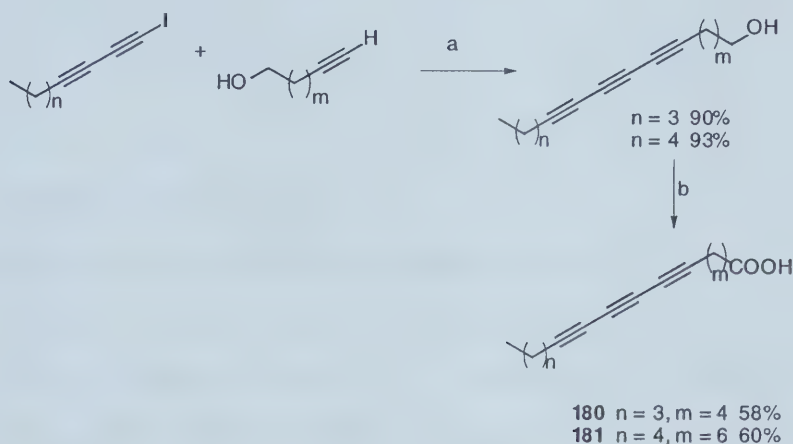
1.3.6. *Heisteria acuminata* (Olacaceae)

The bark of *Heisteria acuminata* (Humb. & Bonpl.) is used in Ecuadorian folk medicine as treatment against toothaches, rheumatism, wounds, and swelling.¹²³ Triynes **180** and **181** and diynes **182–184** have been isolated from the bark of *H. acuminata* and were tested for anti-inflammatory activity.¹²⁴ All five compounds were strong inhibitors of cyclooxygenase (COX), but only acetylenes **182** and **183** showed potent inhibition of 5-lipoxygenase (5-LO) whereas the others showed weak inhibition.¹²⁴



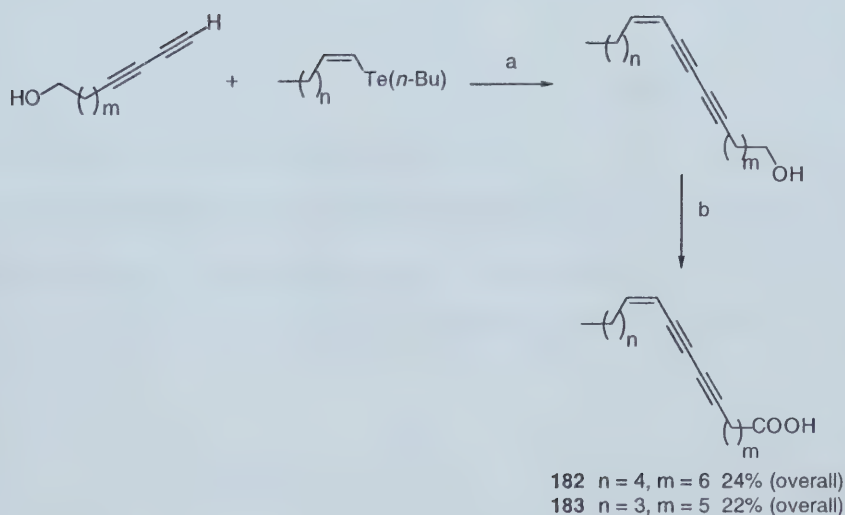
Compounds **180–183** have been synthesized by Zeni, Stefani, et al.¹²⁵ The synthesis of triynes **180** and **181** involved an acetylenic coupling reaction under standard Cadiot–Chodkiewicz conditions using an iododiyne (Scheme 1.16). The formation of ene-diynes **182** and **183** involved a rather interesting twist to Pd-catalyzed cross-coupling method using a vinylic telluride coupling reactions (Scheme 1.17).¹²⁵

Scheme 1.16



(a) CuI , pyrrolidine. (b) $\text{CrO}_3/\text{H}_2\text{SO}_4$, -10°C .

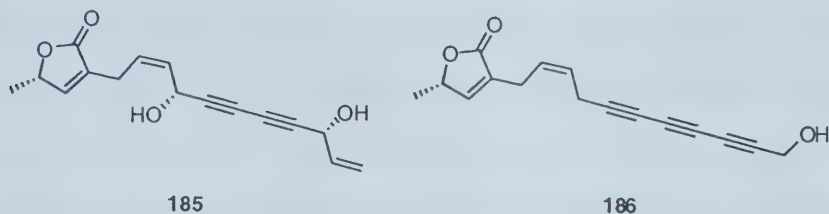
Scheme 1.17



(a) PdCl_2/CuI , $\text{MeOH}/\text{Et}_3\text{N}$. (b) $\text{CrO}_3/\text{H}_2\text{SO}_4$, -10°C .

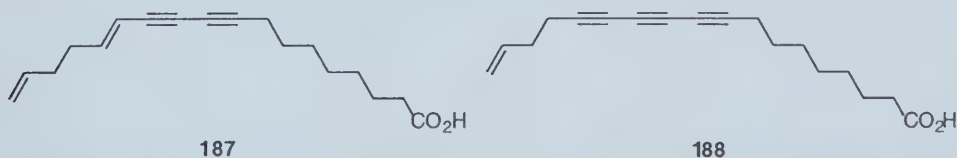
1.3.7. *Lithophyton arboreum*

γ -Lactones **185** and **186** were isolated from the soft corals *Lithophyton arboreum* and *Sarcophyton trocheliophotum*.¹²⁶ While both compounds **185** and **186** were found to be active against Gram-positive bacteria, neither was active against Gram-negative bacteria and yeast.¹²⁶



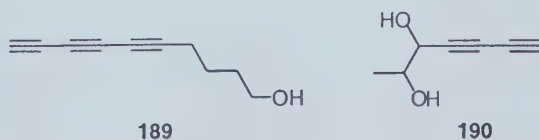
1.3.7. *Mitrephora celebica* (Annonaceae)

Polyacetylene carboxylic acids **187** and **188** have been recently isolated from the stem bark of *Mitrephora celebica*.¹²⁷ Triyne carboxylic acid **188** was previously isolated from the leaves of *Orophea enneandra* Bl.¹²⁸ Compounds **187** and **188** both displayed strong activity against methicillin-resistant *Staphylococcus aureus* and *Mycobacterium smegmatis*.¹²⁷

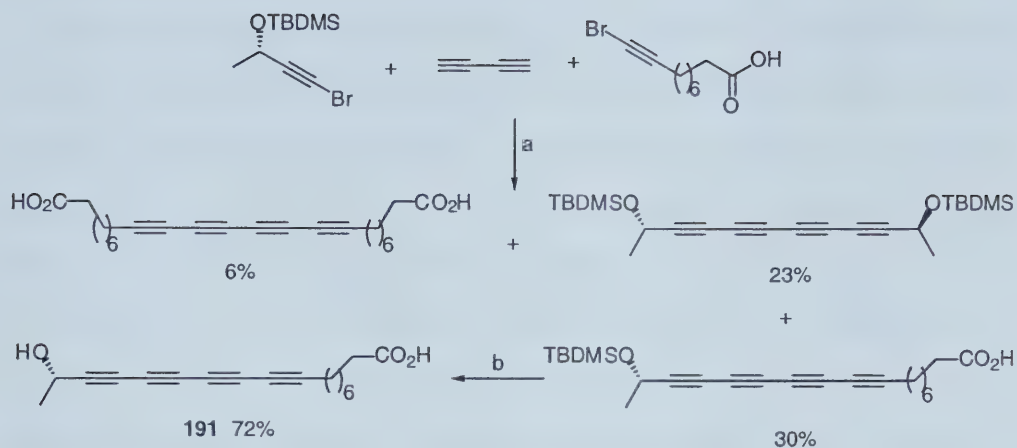


1.3.8. *Psathyrella scobinacea* (Basidiomycetes)

Various natural products were isolated from the culture fluids of the white-rot fungus, *Psathyrella scobinea*.¹²⁹ Among these, novel acetylenic alcohols **189** and **190** were isolated and characterized. The absolute stereochemistry of diyne **190** has not yet been determined.



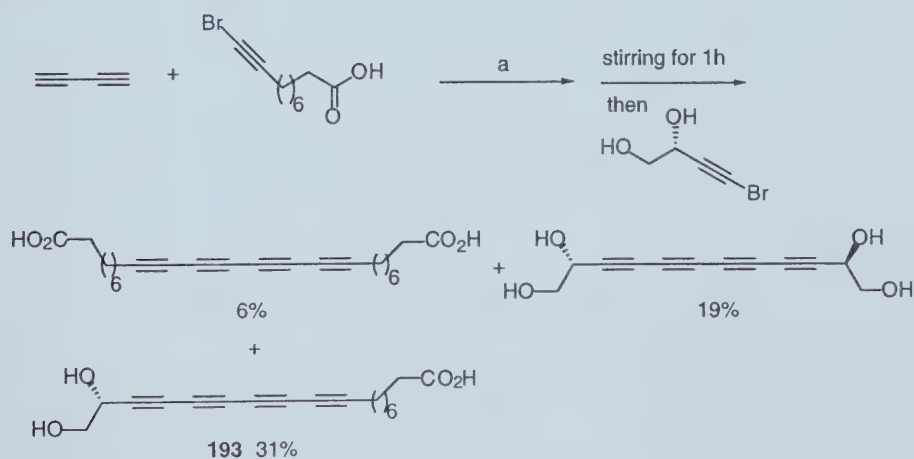
Scheme 1.18



(a) CuCl, EtNH₂, NH₂OH•HCl, MeOH, H₂O, 45 min, 0 °C. (b) HF•Pyr, THF.

Gung et al. have also exploited this one-pot three-component Cadiot–Chodkiewicz reaction for the synthesis of tetrayne **193** (Scheme 1.19).¹³⁶

Scheme 1.19



(a) CuCl, EtNH₂, NH₂OH•HCl, MeOH, H₂O.

1.5. Conclusion and Outlook

Polyacetylenes constitute a very useful class of compounds with important biological activities such as antifungal, antibiotic, anticancer, antitumor, anti-HIV, anti-inflammatory, pesticidal, and antimicrobial properties. Intensive research to isolate new acetylenic compounds and to synthesize naturally occurring acetylenes is an ongoing dynamic process. As can be seen from the syntheses mentioned in this review, a popular method for making natural acetylenic compounds is the Cadiot–Chodkiewicz coupling reaction. We have developed an alternative method that involves an alkylidene carbenoid rearrangement, and in Chapter 3, we demonstrate its applicability to the synthesis of naturally occurring acetylenes. As a preamble to the application of this method to natural product synthesis, we have made a series of diynes and triynes via alkylidene carbenoid rearrangements, and this is discussed in Chapter 2.

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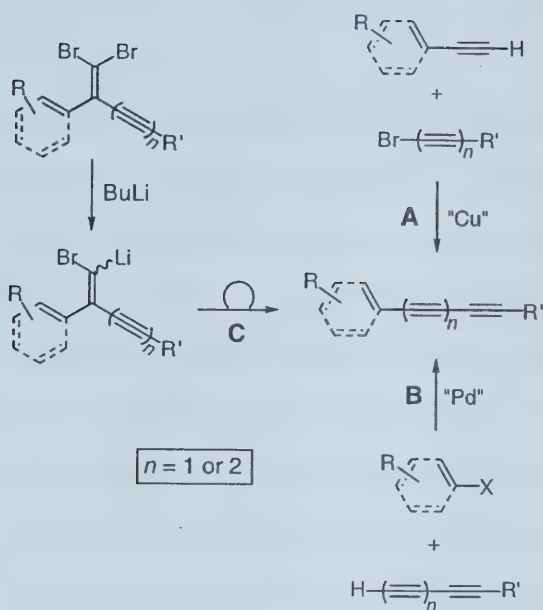
Chapter 2. Synthesis of Unsymmetrically Substituted 1,3-Butadiynes and 1,3,5-Hexatriynes via Alkylidene Carbenoid Rearrangements¹

2.1. Introduction

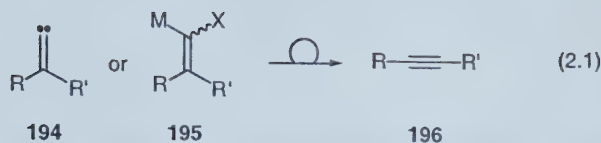
The 1,3-butadiynyl and 1,3,5-hexatriynyl moieties are versatile and useful building blocks in organic synthesis that have been exploited for their rigid and conjugated nature.² Butadiynes, in particular, have been widely utilized as substructures in the formation of new photonic materials,³ oligomers and polymers,⁴ macrocycles,⁵ as well as supramolecular scaffolds.⁶ Diynes and triynes have a rich history as precursors for single crystal polydiacetylene formation via topochemical polymerization reactions, the only method known to give such materials.⁷ Considering that they have a tendency to be unstable, di- and triynes are somewhat surprisingly quite common constituents of natural products.⁸

Symmetrically substituted 1,3-butadiynes are relatively straightforward to synthesize using Hay,⁹ Eglinton/Galbraith,¹⁰ or related protocols, which proceed via oxidative homocoupling of terminal acetylenes with Cu(I)/Cu(II) catalysis.¹¹ These conditions are not suitable, however, for the synthesis of unsymmetrically substituted 1,3-butadiynes. The oxidative coupling of two or more different acetylenic precursors affords a mixture of products, and separation is invariably tedious and difficult. A more substantial challenge is encountered in the formation of both symmetrical and unsymmetrical 1,3,5-hexatriynes via oxidative coupling because the reactivity (acidity) of the two precursors, a terminal acetylene and diacetylene, differ appreciably. Thus, attempts to assemble the triyne skeleton via oxidatively coupling these two groups usually leads first to homocoupling of the diacetylene (to give the symmetrical tetrayne) followed by diyne formation via homocoupling of the acetylene.^{10a,12} Thus, homocoupling is generally an inefficient method for the synthesis of triynes.

Chart 1



As a result of the challenges outlined above for homocoupling reactions, the cross-coupling of terminal acetylenes with alkynyl bromides or iodides, the Cadiot-Chodkiewicz coupling (Chart 2.1, Route **A**),¹³ has often been useful for accessing unsymmetrical 1,3-diyne¹⁴ as well as symmetrical and unsymmetrical 1,3,5-hexatriynes.¹⁵ Such molecules have also been realized via the palladium catalyzed cross-coupling reaction of terminal alkynes with aryl halides or triflates, such as the Sonogashira reaction (Chart 2.1, Route **B**).¹⁶ The predominant limitation of these and related methods in the synthesis of di- and triynes,¹⁷ however, is that they all require the prior synthesis of a terminal alkyne for one, or both, of the coupling partners. This situation becomes problematic in the case of terminal diynes or triynes, which are quite often unstable to isolation and must therefore be generated and utilized in situ.¹⁸



The chemistry of alkylidene carbenes and carbenoid species has a rich and diverse history. Dependent upon reaction conditions and substrate, a free carbene (**194**) can undergo addition reactions to olefins, bond insertion reaction, or as shown in eq 2.1, rearrangements to afford an alkyne **196**. In the case of carbenoid species (**195**), the latter mode of reactivity, rearrangement to an alkyne product, ordinarily dominates; a reaction deemed the Fritsch–Buttenberg–Wiechell (FBW) rearrangement when $\text{R} = \text{R}' = \text{aryl}$.¹⁹ This transformation has been a well-utilized technique for the formation of tolans.^{20,21} Eisler and Tykwinski have recently described the modification of this method and have demonstrated that it is suitable for the formation of polyynes via alkyne migration in carbene/carbenoid intermediates.^{22,23} These initial studies suggested that, in addition to the well-established propensity for aryl and olefin migration in an alkylidene carbenoid species,^{20b} 1,2-alkyne migrations could also be quite successful. As a result, we envisioned 1,1-dibromoolefins as precursors to di- and triynes **196** as shown in Chart 2.1, Route C. This reaction would involve a sequence of lithium–halogen exchange with a suitable 1,1-dibromoolefin to give the carbene/carbenoid intermediate, followed by rearrangement to the desired polyne.

Described herein is the successful synthesis of functionalized, unsymmetrical 1,3-butadiynes²⁴ and 1,3,5-hexatriynes via this method.²⁵ Beginning with commercially available aryl or vinyl aldehydes and carboxylic acids (or acid chlorides), these polyynes are achieved in four facile steps, with the carbenoid rearrangement proceeding under mild conditions and generally in good to excellent yields. As this method has not been successfully executed in all cases, however, the scope and limitation of this protocol are also discussed.

2.2. Results and Discussion²⁶

The synthetic sequence toward unsymmetrically substituted 1,3-butadiynes begins with condensation of a lithium acetylide with an aryl or vinyl aldehyde as outlined in Scheme 2.1.²⁷ A slight excess of the appropriate acetylene **197** is lithiated with *n*-BuLi at $-78\text{ }^{\circ}\text{C}$ in Et_2O to give the corresponding lithium acetylide, and the aryl carboxaldehyde (1 equiv) is added neat at $-78\text{ }^{\circ}\text{C}$. The reaction mixture is slowly warmed to ca. $-10\text{ }^{\circ}\text{C}$ until the reaction is judged complete by TLC. The solution is cooled again to $-78\text{ }^{\circ}\text{C}$ and quenched with aqueous NH_4Cl . As a result of the slight excess of the acetylide, complete reaction with the aldehyde can generally be effected, and the resultant alcohols **198** can be isolated pure and in high yield following aqueous work-up (Table 2.1).

Scheme 2.1

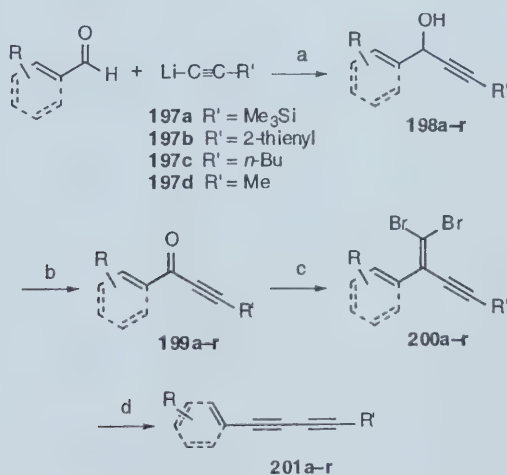
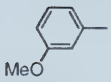
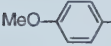
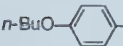
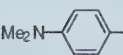
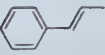
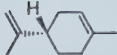
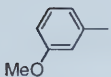


Table 2.1. Isolated yields for compounds **198–201**.

compd	R	R'	198 yield (%) ^a	199 yield (%)	200 yield (%)	201 yield (%)
a		Me ₃ Si	64	— ^a	44 ^{c,d}	93
b		Me ₃ Si	96	83 ^a	39 ^{c,e}	79
c		Me ₃ Si	90	— ^a	59 ^{c,d}	43
d		Me ₃ Si	76	76 ^a	48 ^{c,d}	75
e		Me ₃ Si	97	— ^a	47 ^{c,d}	82
f		Me ₃ Si	69	— ^a	38 ^{c,e}	79
g		Me ₃ Si	91	—	—	—
h		Me ₃ Si	85	— ^a	34 ^{c,d}	54
i		Me ₃ Si	97	87 ^a	85 ^d	91
j		Me ₃ Si	50	—	—	—
k		Me ₃ Si	95	36 ^a 94 ^b	26 ^{c,e}	28
l		Me ₃ Si	81	96 ^b	77 ^{c,d}	95
m		Me ₃ Si	63	85 ^b	27 ^d	46
n		Me ₃ Si	39	89 ^b	—	—

o			80	35 ^a 82 ^b	—	—
p		<i>n</i> -Bu	88	46 ^a	7 ^{c,d}	92
q		<i>n</i> -Bu	94	82 ^a	16 ^{c,d}	86
r		Me	98	73 ^a	17 ^d	41

^aUsing PCC in CH₂Cl₂. ^bUsing BaMnO₄ in CH₂Cl₂. ^cYield over two steps from alcohol, without isolation of intermediate ketone. ^dDibromoolefination reaction in CH₂Cl₂ at rt.
^eDibromoolefination reaction in C₆H₆ at 80°C.

Oxidation from alcohol **198** to ketone **199** is normally accomplished with PCC at room temperature in CH₂Cl₂. Reaction times are less than 1 h for most derivatives. Concentration of the reaction mixture, followed by filtration through a short plug of silica affords the crude ketone. The ketone is normally of sufficient purity to be carried on to the subsequent dibromoolefination step. The ketones can, however, be isolated pure by column chromatography, as demonstrated for a number of the examples in Table 2.1. The oxidation of several alcohols was particularly difficult with PCC (e.g., **198k**, **198n**, **198o**). As a result, BaMnO₄ was employed as the oxidant,²⁸ with more satisfactory results. As this reaction is done in CH₂Cl₂, filtration of the reaction solution through Celite to remove the insoluble barium salts affords a CH₂Cl₂ solution of the ketone suitable to be carried on to the dibromoolefination step without additional purification or manipulation. In two cases, the aniline and pyridine derivatives **198g** and **198j**, we were unable to successfully complete the oxidation procedure due to the chemical instability of these substrates.

The well-established dibromoolefination method using PPh₃/CBr₄ was employed to provide derivatives **200**.²⁹ For sterically unhindered ketones, the dibromoolefinations

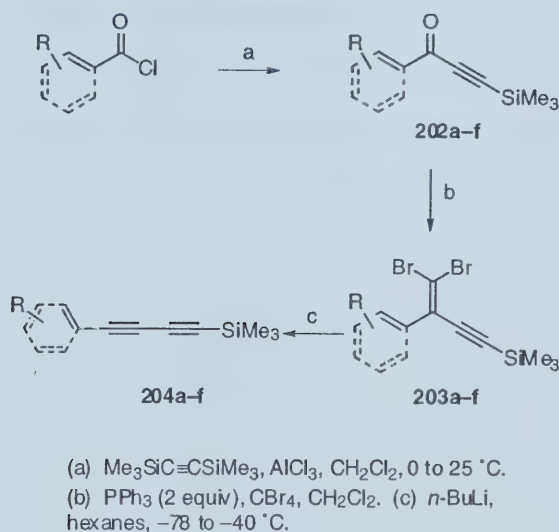
can generally be completed at room temperature in CH_2Cl_2 in 1-2 hours. For ketones **199b**, **199f**, and **199k**, however, reactions were sluggish at rt in CH_2Cl_2 and were therefore carried out in benzene under reflux. In all cases, the dibromoolefinic products are considerably less polar than the ketone precursors, as well as any by-products of the reaction, and can therefore be quickly and easily purified by column chromatography on silica.

During the course of this study, it became apparent that the dibromoolefination step is the weakest link in this synthetic sequence. The first 1,3-butadiyne derivatives that we targeted were terminated at one end with a trimethylsilyl group (entries **a-n**, Table 2.1) since this alkyne protecting group nicely allows for further synthetic elaboration of the resultant diynes. In these cases, reasonable to good yields of the desired dibromoolefinic products could be achieved, whether beginning with either the pure ketone or the crude product directly from the oxidation reaction. As it turns out, however, the presence of the trimethylsilyl group also appears to play a significant role in the success of the dibromoolefination reactions. In cases when this group has been replaced by either an alkyl or aryl moiety, the yields from dibromoolefination reaction are dramatically reduced (e.g., **200p-r**) and in some cases we have been unable to effect this transformation at all (entries **200n** and **200o**). To date, this remains the predominant limitation of our methodology, and we are actively exploring possible solutions to this obstacle.

The conversion of the dibromoolefins **200** to the desired diynes **201** has been consistently more successful in hexanes, as opposed to more polar solvents such as Et_2O or THF.^{30,31} Thus, diyne formation is effected by the dropwise addition of *n*-BuLi to a hexanes solution of **200** cooled to $-78\text{ }^\circ\text{C}$. The mixture is subsequently warmed to ca. $-40\text{ }^\circ\text{C}$ over 0.5 hr to ensure complete rearrangement of the carbenoid intermediate³² and then quenched by the addition of an aqueous NH_4Cl solution. If rigorously anhydrous reaction conditions have been maintained during the rearrangement, the diyne is generally

the sole product as observed by TLC analysis.³³ The diynes can thus be isolated pure, in good to excellent yields, by passing the concentrated reaction mixture through a plug of silica to remove any polar baseline material. As demonstrated in Table 2.1, the carbenoid rearrangement process allows a range of pendant groups to be appended to the diyne skeleton, including aromatic hydrocarbon (**201a–b**), electron rich and poor aryl (**201c–f**, **k**, **p**),³⁴ heteroaryl (**201h**, **i**, **q**, **r**), alkyl (**201p–r**), and vinyl (**201l**, **m**) functionality.

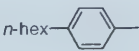
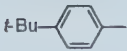
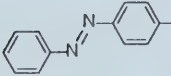
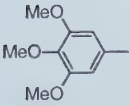
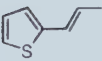
Scheme 2.2



Scheme 2.2 outlines an alternate pathway to aryl 1,3-diynes that exploits readily available carboxylic acid chlorides. Friedel-Crafts acylation of aryl or vinyl acid chlorides with bis(trimethylsilyl)acetylene in the presence of AlCl_3 in CH_2Cl_2 at 0 °C easily afforded ketones **202a–f** in good to excellent yields (Table 2.2).³⁵ Dibromoolefination of **202a–f** under standard conditions generated **203a–f**. Subjecting dibromides to $n\text{-BuLi}$ at -78 °C according to the standard protocol described above afforded **204a–e** in good to excellent yields. This route allowed formation of functionalized diacetylenes such as the azo-diyne **204c**, trimethoxyarene **204d**, as well as thienyl terminated enediyne **204e**. Frustratingly, rearrangement of butadienyl derivative

203f was unsuccessful, regardless of conditions employed. For this substrate, unreacted dibromoolefin **203f** was recovered, along with the product derived from protonation of the intermediate carbenoid species, but no diyne could be detected in the reaction mixture. In view of the facile rearrangement of vinyl dibromides **203l**, **203m**, and **203e**, the inability to effect an analogous rearrangement on **203f** is surprising and remains unexplained. Possible improvements to make the rearrangement of **203f** proceed may be to use a larger amount of *n*-BuLi, and to carry out the reaction at warmer temperatures, e.g. starting at $-40\text{ }^{\circ}\text{C}$ and warming the reaction to rt.

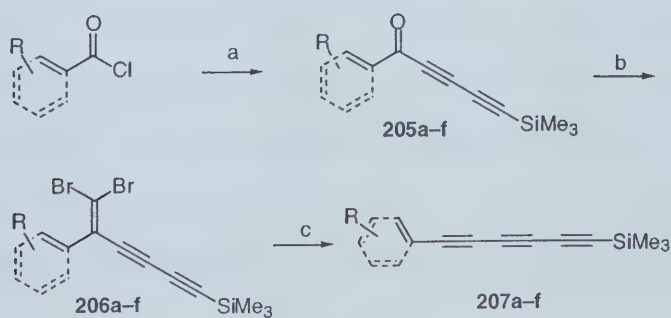
Table 2.2. Isolated yields for compounds **202–204**.

compd	R	202 yield (%)	203 yield (%)	204 yield (%)
a		90	79	70
b		78	61	88
c		43	83	61
d		91	91	51
e		62	67	55
f		66	41	—

The traditional difficulties encountered in the synthesis of unsymmetrical triacetylenes led us to extend our general protocol in this direction, as outlined in Scheme 2.3. Friedel-Crafts acylation of the appropriate acyl chloride with 1,4-bis(trimethylsilyl)-1,3-

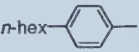
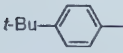
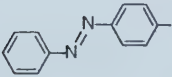
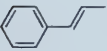
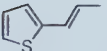
butadiyne provided diynones **205a–f** (Table 2.3). Ketones **205a–c**, with pendant aryl functionality, showed somewhat limited stability. Although they could be isolated, decomposition was always observed when manipulations were carried out under ambient conditions. Thus, these compounds were expeditiously carried on to the dibromoolefination step in CH_2Cl_2 at rt, following work-up. Although the dibromoolefinic products **206a–c** are relatively stable, overall yields for these derivatives remained low for the two-step process. Conversely, enediynones **205d–f** were considerably more stable and could be isolated in good yields and characterized in all cases. The enhanced stability of **205d–f** also afforded increased yields for dibromoolefins **206d–f**, which were isolated in 40–75% yield. Carbenoid rearrangement of **206a–f** to triynes **207a–f** was accomplished in the same manner as outlined for diyne formation above. Yields from these rearrangements were moderate to excellent, with olefinic derivatives consistently formed in higher yields. It should be noted that unlike the formation of azo-diyne **204c**, which proceeded without isomerization of the azo moiety, triyne **207c** was isolated and characterized as a mixture of its *E*- and *Z*-stereoisomers.

Scheme 2.3



(a) $\text{Me}_3\text{SiC}\equiv\text{C}-\text{C}\equiv\text{CSiMe}_3$, AlCl_3 , CH_2Cl_2 , 0 to 25 °C. (b) PPh_3 (2 equiv), CBr_4 , CH_2Cl_2 . (c) *n*-BuLi, hexanes, –78 to –40 °C.

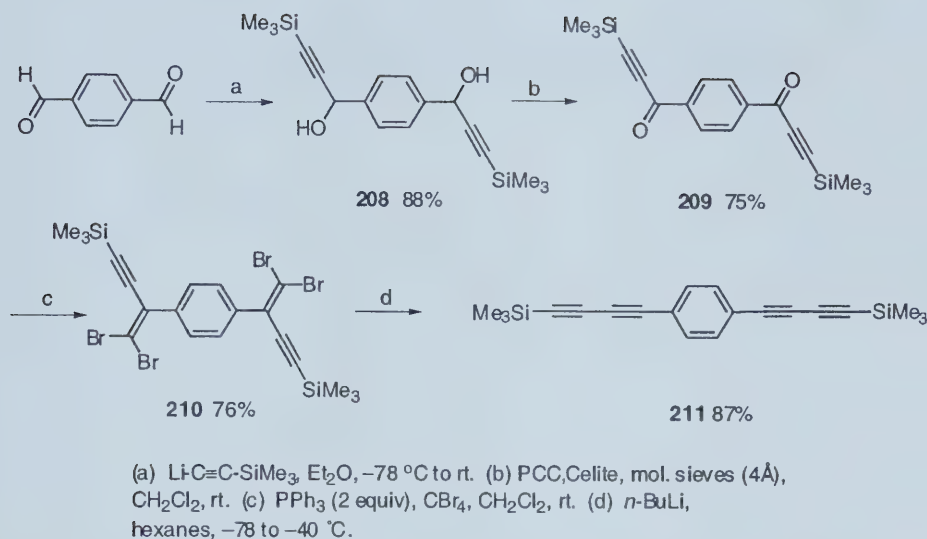
Table 2.3. Isolated yields for compounds **205–207**.

compd	R	205 yield (%)	206 yield (%)	207 yield (%)
a		—	21 ^a	41
b		—	24 ^a	98
c		—	8 ^a	46
d		45	72	82
e		69	75	74
f		65	40	76

^aYield over two steps from acid chloride, without isolation of intermediate ketone.

This general sequence of reactions is applicable to the assembly of larger, extended polyynes systems as outlined in Scheme 2.4. Diol **208** is easily produced in 88% yield as a mixture of stereoisomers via the condensation of $\text{Li}-\text{C}\equiv\text{C}-\text{SiMe}_3$ with terephthalaldehyde. Oxidation with PCC, followed by dibromoolefination gave the tetrabromide **210** in 56% yield over the two steps from **208**. Subjecting **210** to 2.4 equiv of *n*-BuLi afforded 1,4-bis(4-trimethylsilyl-1,3-butadiynyl)benzene **211** in 87% yield as a colorless, quite stable, crystalline solid. The formation of **211** nicely demonstrates the ability to scale-up the rearrangement protocol: this reaction produced nearly 2 g of **211**.

Scheme 2.4



Single crystals of **211** were easily grown from a concentrated solution in hexanes at 4°C . X-ray crystallographic analysis of **211** shows the butadiynyl segments to be nearly linear, as expected for an sp -hybridized carbon system (Figure 2.1). The most notable feature of the solid state structure is the parallel solid-state alignment of neighboring molecules, in a manner potentially suitable for topochemical polymerization. Analysis of the packing parameters shows that the stacking angle between neighboring molecules is $\theta = 49^\circ$, near the optimal value of 45° required for a 1,4-polymerization process.³⁶ The stacking distance at $d = 5.9 \text{ \AA}$ and distance between reacting atoms $R = 4.4 \text{ \AA}$ (C7 to C4 of neighboring molecule), however, are both outside the ideal values of $d \sim 5 \text{ \AA}$ and $R < 4 \text{ \AA}$, respectively. Thus, the observed stability of **211** in the solid state can be attributed, at least in part, to the inability of the compound to undergo topochemical polymerization.

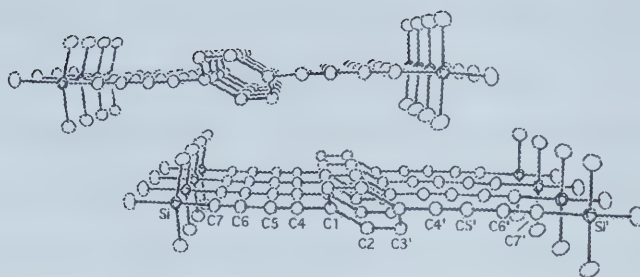


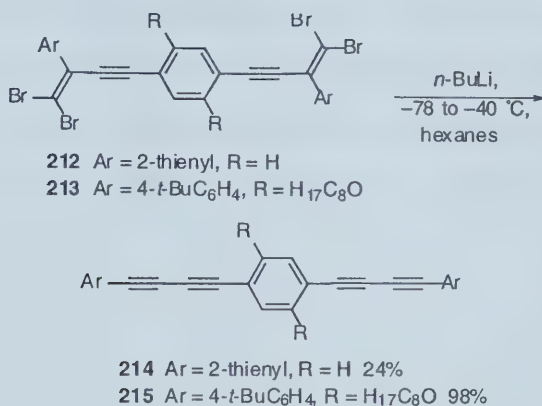
Figure 2.1. ORTEP drawing (20% probability level) of **211** demonstrating solid-state packing. Selected bond lengths (Å) and angles (°): C(1)-C(4) 1.432(3), C(4)-C(5) 1.196(3), C(5)-C(6) 1.377(3), C(6)-C(7) 1.208(3); C(1)-C(4)-C(5) 178.8(2), C(4)-C(5)-C(6) 178.7(2), C(5)-C(6)-C(7) 179.6(2), C(6)-C(7)-Si 178.57(19).

The synthesis of two functionalized, extended polyyne systems are described Scheme 2.5. Tetrabromide **212** derives from the condensation of the bis(lithium) acetylide of 1,4-(diethynyl)benzene with 2-thiophene carboxaldehyde, followed by PCC oxidation and dibromoolefination under standard conditions. The tetrabromide **212** was isolated in 33% yield, over two steps from the diol, with the moderate yield primarily the result of the problematic isolation of the relatively insoluble solid **214** from the reaction mixture. Rearrangement of tetrabromide **212** to tetrayne **214** was accomplished by the addition of *n*-BuLi at -78°C and then allowing the reaction mixture to warm to approximately -10°C to increase the solubility of **212** and facilitate the rearrangement. The rigid tetrayne **214** proved to be a nearly insoluble solid, which hampered isolation and purification. Nonetheless, it could be obtained in 24% yield as a yellow solid that has been identified by its ^1H NMR spectrum, which demonstrates its symmetrical structure and by mass spectrometry, which shows the expected parent signal at m/z 338.

The tetrabromide **213** is obtained as a stable oil via the two-step sequence of the Friedel-Crafts acylation of 1,4-di(octyloxy)-2,5-bis(trimethylsilylethynyl)benzene with 4-*t*-butylbenzoyl chloride, followed by dibromoolefination in CH_3CN . Although the

octyloxy side chains and the *tert*-butyl end groups greatly enhanced the solubility of **213**, yields from the dibromoolefination step remained frustratingly low (~20%), regardless of the conditions employed. Solubility did, however, have a dramatic effect on the yield of the rearrangement step, and the highly fluorescent, stable tetrayne **215** was produced in nearly quantitative yield from tetrabromide **213**. Somewhat surprisingly, **215** is a solid, despite the presence of both the *tert*-butyl and octyloxy groups.

Scheme 2.5



2.3. Conclusions and Prospects

In summary, the modified FBW rearrangement described herein provides a facile route to a range of aryl diyne and triyne systems. This synthetic route offers several attractive features versus more commonly employed palladium coupling methods including (1) the wide range of commercially available aryl and vinyl aldehydes and carboxylic acid precursors, (2) tolerance of a range of chemical functionality, (3) generally rapid reaction times and easy purification/isolation that often allow for all four transformations of the di- or triyne synthesis to be accomplished within a single day. The most significant limitation of this method, to date, is the variability encountered in the conversion of ynones into the requisite dibromoolefinic precursors. Whereas this step generally

proceeds in good yield for derivatives of trimethylsilyl substituted substrates, other end groups are not as well tolerated.

In cases where the trimethylsilyl group was substituted by alkyl groups, drastically lower yields were obtained for the dibromoolefination step. Different conditions were used in an attempt to improve the yield in the conversion of ketone **199r** into dibromoolefin **200r**. Use of triethylamine as additive,³⁷ as well as substitution of one mole equivalent of triphenylphosphine with zinc metal and stirring for 24 hours^{29a} did not improve the yields. Likewise, changing the solvent from dichloromethane to benzene or acetonitrile did not provide any noticeable improvement in the reaction. An alternative dibromoolefination method using dibromomethylene triphenylphosphonium bromide and potassium *tert*-butoxide in THF³⁸ was attempted but was ineffective.

2.4. References

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(32) Using TLC to monitor these reactions is problematic, as warming of the sample in the capillary tube used for TLC application can lead to the inaccurate observation that the reaction has reached completion.

(33) The importance of rigorously anhydrous conditions cannot be overemphasized. A practical aspect of maintaining anhydrous conditions is to avoid introducing any water in

the reaction through the use of any sample of the dibromoolefin precursor that has been utilized for NMR analysis, considering that the deuterated solvent used in preparing the solution sample inevitably contains a small amount of water.

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Chapter 3. Synthesis of Naturally Occurring Acetylenes via an Alkylidene Carbenoid Rearrangement¹

3.1. Introduction

Mosquito larvicidal agents are important in the fight to eradicate mosquito-borne diseases such as the West Nile Virus, malaria, and dengue fever.² The allure of naturally occurring toxins for this purpose is attributable to their biodegradability and the fact that they generally leave no long-lived residues.³ As outlined in Chapter 1, naturally occurring acetylenes⁴ have been isolated from a wide variety of plant species,³ cultures of higher fungi,^{3a-c,5} and marine sponges,⁶ and have proven to be important biologically active compounds due to their antibacterial, antimicrobial, antifungal, and insecticidal properties.^{2,7} The natural products **216** and **167** illustrate the potency of certain acetylenes, and both are extremely phototoxic toward mosquito larvae.⁸ Ene-triyne **216** was first isolated by Bohlmann et al. from various *Chrysanthemum* plant species.⁹ Biological studies conducted on compound **216** revealed it to be highly phototoxic toward *Aedes atropalpus* larvae and *Aedes aegypti* larvae, with LC₅₀ values of 0.100 ppm and 0.079 ppm, respectively. Compound **216** was also phototoxic to blackfly larvae and adult nematodes.^{7b} 1-Phenylhepta-1,3,5-triyne (**167**) has been isolated from diverse plant species, such as *Bidens pilosa* L. (Asteraceae),¹⁰ and several members of the *Coreopsis* family.^{8b} Triyne **167** has been extensively studied and displays insecticidal activity (LC₅₀ 204 ng/cm²) on first instar larvae of the fall armyworm *Spodoptera frugiperda* Smith, phototoxicity toward *Aedes aegypti* larvae, antimicrobial activity, ovicidal activity against *Drosophila melanogaster*, and nematocidal activity.^{7b,c,11} Diene-diyne **12**, atractylodin, has previously been isolated from the rhizomes of various *Atractylodes* species,¹² and is phototoxic and antibiotic against *Escherichia coli*, *Saccharomyces cerevisiae* and *Candida albicans*,^{11c} but it has not yet been tested for mosquito larvicidal activity. Ene-

diyne **217**, 2-hept-1-ene-3,5-diynylfuran, is a novel synthetic compound that has been synthesized in view of its potential as a mosquito larvicidal agent due to its structural analogy to compound **216**.

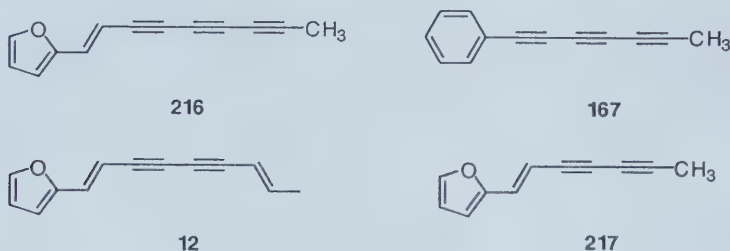


Figure 3.1. Structures of synthetic targets.

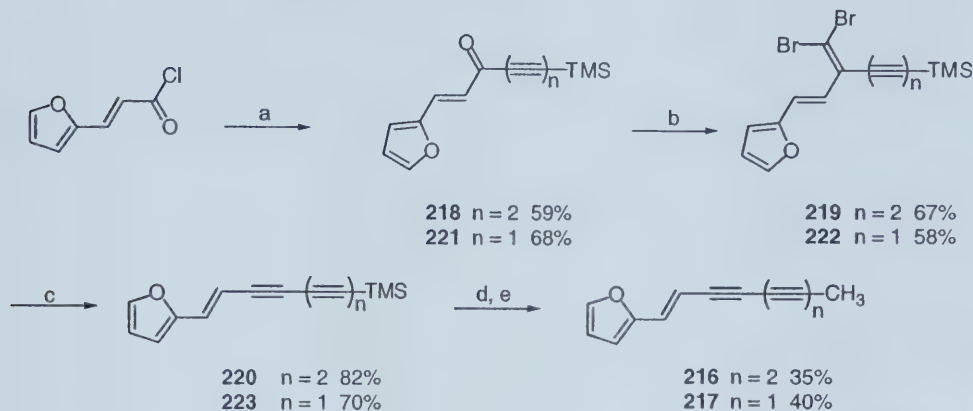
In this chapter, we present the synthesis of acetylenes **12**,¹³ **167**,¹⁴ **216**,¹⁵ and **217** via a modification of the Fritsch–Buttenberg–Wiechell rearrangement¹⁶ described in Chapter 2.¹⁷ The synthesis of the dibromoolefin precursors is easily achieved in three procedurally facile steps from commercially available carboxylic acids or aldehydes, rendering this route a viable alternative to previous methods for acetylenic natural product synthesis.^{12–14}

3.2. Results and Discussion

Ene-triyn **216** was synthesized as shown in Scheme 3.1. The first step in this reaction scheme involved a Friedel–Crafts acylation of 3-(2-furyl)acryloyl chloride with 1,4-bis(trimethylsilyl)-1,3-butadiyne to give the ketone **218**. Dibromoolefination then produced compound **219**. Fritsch–Buttenberg–Wiechell rearrangement of dibromoolefin **219** using *n*-BuLi at $-78\text{ }^{\circ}\text{C}$ in hexanes as solvent then gave the ene-triyn **220** in 82% yield. Protodesilylation of **220** using K_2CO_3 afforded the corresponding

terminal ene-triyn which was then converted to the lithium acetylide. Methylation with methyl iodide gave the target ene-triyn **216** (11% overall yield).¹⁸

Scheme 3.1



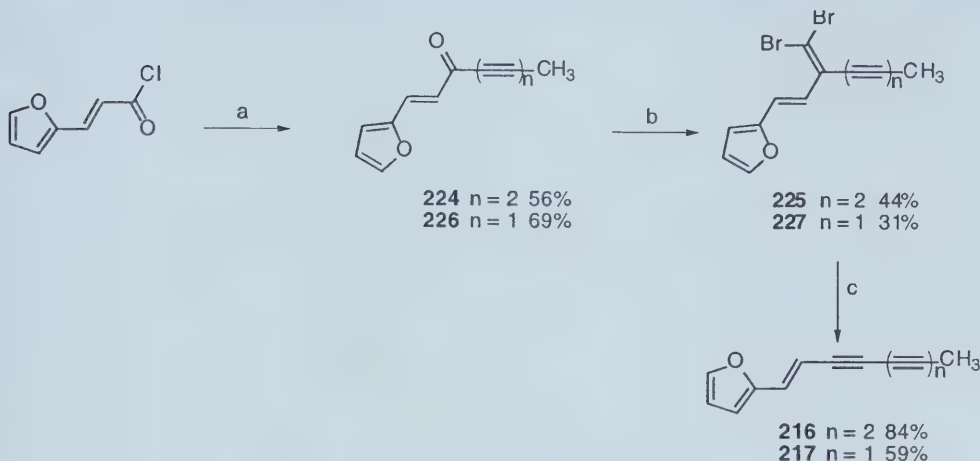
(a) $\text{Me}_3\text{Si}(\text{C}\equiv\text{C})_n\text{SiMe}_3$, AlCl_3 , CH_2Cl_2 , 0 °C. (b) PPh_3 (2 equiv), CBr_4 , CH_2Cl_2 , rt. (c) $n\text{-BuLi}$, hexanes, -78 to -40 °C. (d) K_2CO_3 , MeOH/THF . (e) $n\text{-BuLi}$, THF , -78 °C, then MeI , -78 °C to rt.

Likewise, the diyne analogue of compound **216**, 2-hept-1-ene-3,5-diynylfuran (**217**), was synthesized via a similar sequence of Friedel–Crafts acylation to provide ketone **221**, dibromoolefination to **222**, and rearrangement to **223**. Protidesilylation of **223**, lithiation of the corresponding terminal ene-diyne, and subsequent methylation furnished **217** in 11% overall yield.

Clearly, the weakest step in the above scheme involves methylation of the unstable terminal alkyne to afford either **216** or **217**, so a more effective synthetic pathway for targets **216** and **217** was explored (Scheme 3.2). Friedel–Crafts acylation with trimethylsilylpenta-1,3-diyne¹⁹ gave the ketone **224** directly from 3-(2-furyl)acryloyl chloride. Dibromoolefination provided **225**, and rearrangement produced the desired

product, ene-triyne **216**, in 84% yield. This amounted to an overall yield of 21%, a two-fold increase relative to the previous synthetic scheme for compound **216**.

Scheme 3.2

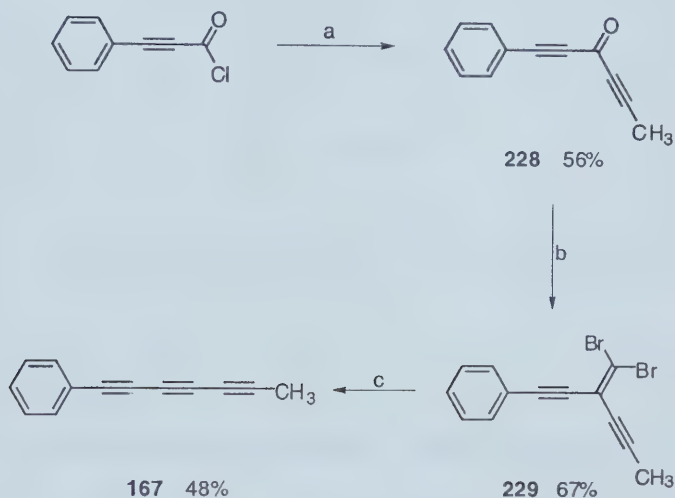


(a) $\text{Me}_3\text{Si}(\text{C}\equiv\text{C})_n\text{Me}$, AlCl_3 , CH_2Cl_2 , 0°C . (b) PPh_3 (2 equiv), CBr_4 , CH_2Cl_2 , rt. (c) $n\text{-BuLi}$, hexanes, -78 to -40°C .

Similarly, ene-diyne **217** was synthesized via a sequence of Friedel–Crafts acylation with trimethylsilylpropyne to produce the ketone **226**, dibromoolefination to give **227**, and carbenoid rearrangement of **227** to afford the desired product **217** in 59% yield. Thus, the overall yield of 13% is slightly higher than that for the previous synthetic route and consists of one less step. Somewhat surprising is the fact that dibromoenes **222** and **227** are less stable than their diyne counterparts **219** and **225**, which ultimately lowers the overall yield of **217** in both cases. Considering the high instability of the dibromoenes **222** and **227**, it would be advisable to make use of these dibromoenes within a couple of days from isolation as these compounds both tend to decompose within hours at rt, and within days when kept refrigerated below 4°C , even when stored in solution and protected from exposure to light.

1-Phenylhepta-1,3,5-triyne (**167**) was synthesized (Scheme 3.3) starting from a Friedel–Crafts acylation reaction of phenylpropiolyl chloride with trimethylsilylpropyne, giving ketone **228** in 56% yield.²⁰ Dibromoolefination yielded compound **229** (67%), and subjecting **229** to *n*-BuLi produced 1-phenylhepta-1,3,5-triyne (**167**) in 18% overall yield.

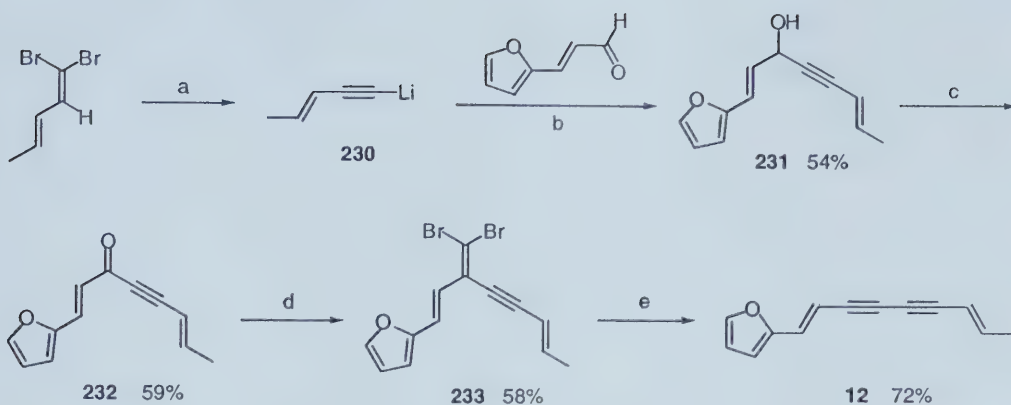
Scheme 3.3



(a) $\text{Me}_3\text{SiC}\equiv\text{CMe}$, AlCl_3 , CH_2Cl_2 , 0°C . (b) PPh_3 (2 equiv), CBr_4 , CH_2Cl_2 , rt. (c) *n*-BuLi, hexanes, -78 to -40°C .

The synthesis of atractylodin (**12**) is outlined in Scheme 3.4. The lithium acetylide **230** was generated from 1,1-dibromo-1,3-pentadiene²¹ and reacted with 2-furanacrolein to give alcohol **231** (54% yield over two steps). Oxidation of **231** to ketone **232**, followed by dibromoolefination, yielded compound **233** (58%).²² Finally, rearrangement of the dibromoolefin **233** gave atractylodin (**12**) in 13% overall yield.

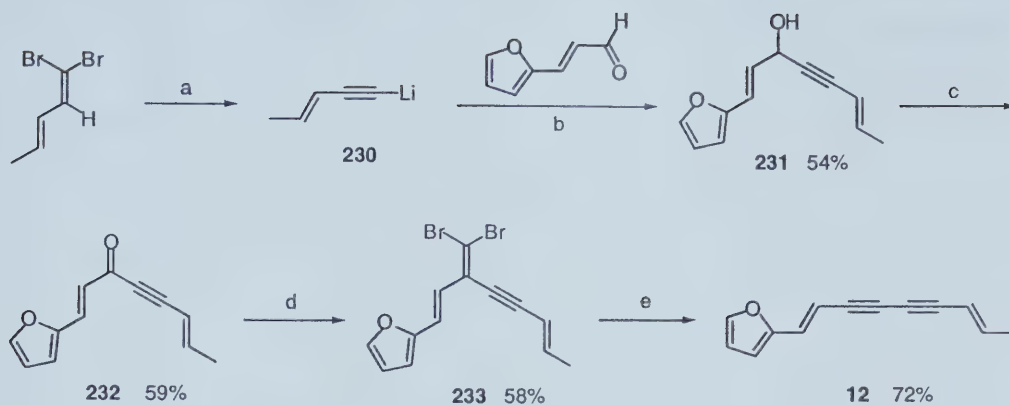
Scheme 3.4



3.3. UV-vis spectra

The UV-vis spectra obtained for compounds **216** and **12** (Figure 3.2) were diagnostic of a furyl ene-triyne and a furyl ene-diyne-ene system, respectively. Similarly, the UV-vis spectrum obtained for phenylheptatriyne (**167**) (Figure 3.3) was typical of an aromatic triynyl system. Moreover, the UV-vis data for all three compounds were consistent with literature values.^{9a,11a,13,23}

Scheme 3.4



3.3. UV-vis spectra

The UV-vis spectra obtained for compounds **216** and **12** (Figure 3.2) were diagnostic of a furyl ene-triyne and a furyl ene-diyne-ene system, respectively. Similarly, the UV-vis spectrum obtained for phenylheptatriyne (**167**) (Figure 3.3) was typical of an aromatic triynyl system. Moreover, the UV-vis data for all three compounds were consistent with literature values.

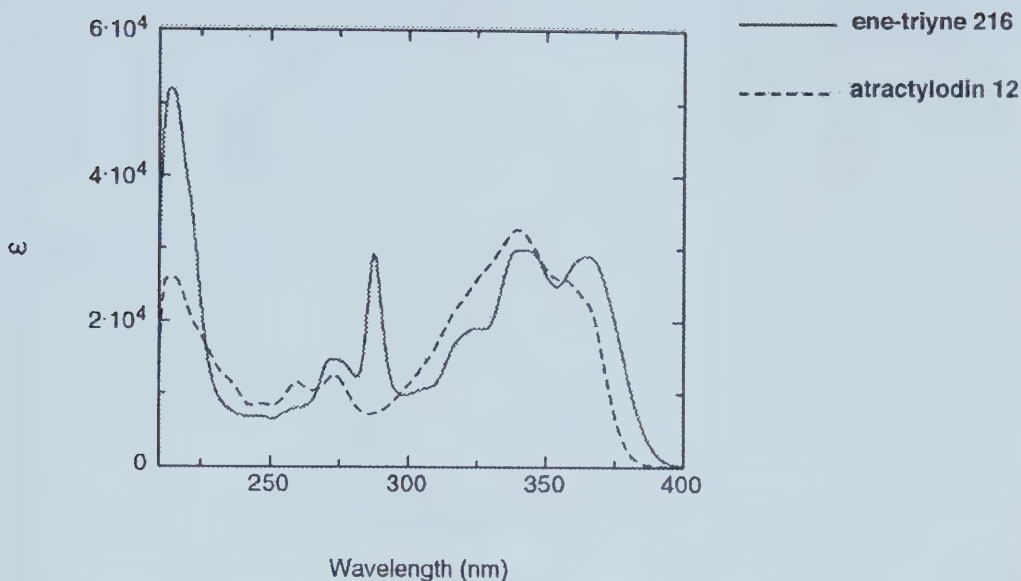


Figure 3.2. UV-vis spectra for compounds **12** and **216**.

3.4. Conclusions

The applicability of an alkylidene carbenoid rearrangement toward the synthesis of naturally occurring acetylenes and their analogues has been demonstrated by the total synthesis of acetylenes **12**, **167**, **216** and **217**. The usefulness of this method is emphasized by the fact that the dibromoolefin precursors of this reaction can be easily realized from commercially available carboxylic acids and aldehydes. This feature eliminates the need for unstable acetylenic precursors commonly required for other routes.

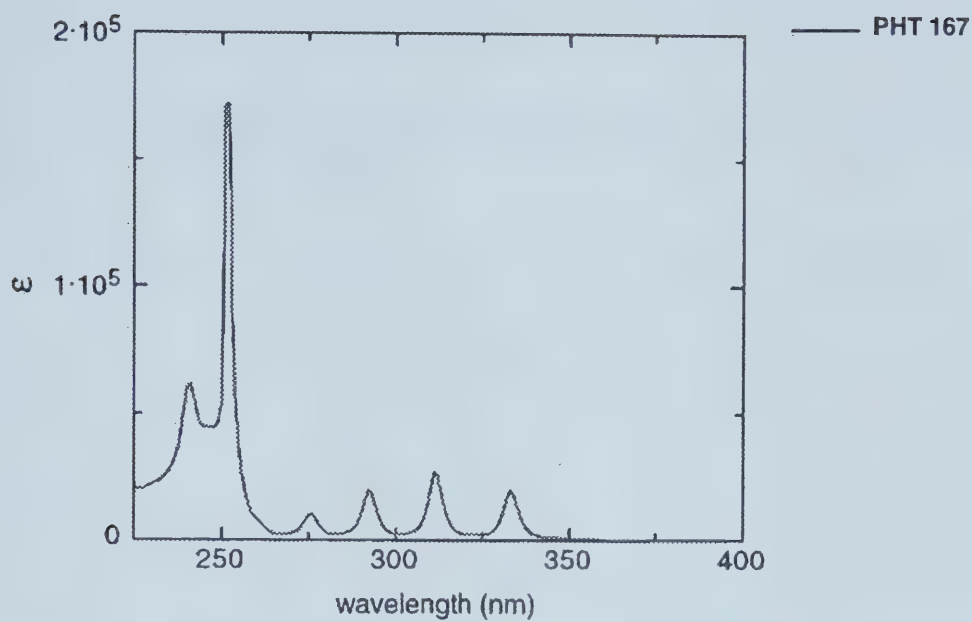


Figure 3.3. UV-vis spectrum for compound 167.

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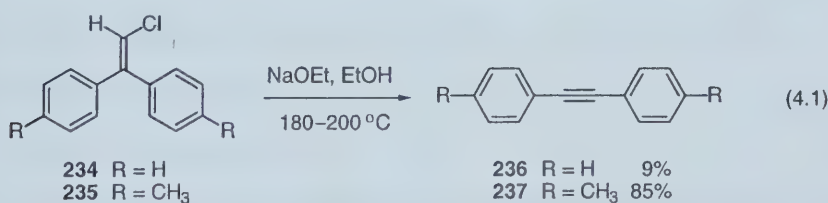
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Chapter 4. Mechanistic Investigation of the Modified

Fritsch–Buttenberg–Wiechell Rearrangement

4.1. Introduction

The original Fritsch–Buttenberg–Wiechell (FBW) rearrangement was conceived in 1894, and it involved treatment of 1,1-diaryl-2-chloroethylenes with sodium ethoxide in ethanol at 180–200 °C resulting in a 1,1-elimination reaction and a subsequent rearrangement to yield substituted tolans (Equation 4.1).^{1,2} In a related reaction, Tiffeneau reported several years later that 1-bromo-2-phenylpropene was converted to 1-phenylpropyne using molten potassium hydroxide.³ The formation of diarylacetylenes by FBW rearrangement of chloro- and bromoolefins can also be carried out under milder conditions using potassium amide in liquid ammonia.⁴ Reaction of 1,1-diphenyl-2,2-dichloroethylene with sodium in benzene⁵ or with phenyllithium in ether⁶ also yielded diphenylacetylene.



A variant of the FBW rearrangement has been developed in our research group by Eisler and Tykwinski⁷ and has been discussed in Chapters 2 and 3. This modified FBW rearrangement involves α -elimination of 1,1-dibromoolefins using *n*-BuLi at low temperatures followed by rearrangement of the resulting carbenoid intermediate to yield the desired polyynes.⁷ Having demonstrated the applicability of this methodology to the synthesis of a wide range of polyynes, we now turned our attention to the mechanism of the rearrangement process. Different mechanistic considerations were involved: (1) the nature of the intermediate (carbene or carbenoid?), (2) the migrating group, and the relative migratory aptitudes of the different functionalities, (3) the regiospecificity, or lack

thereof, of the lithium-halogen exchange, and (4) the stereospecificity of the rearrangement (*cis* or *trans* migration relative to the halogen or both).

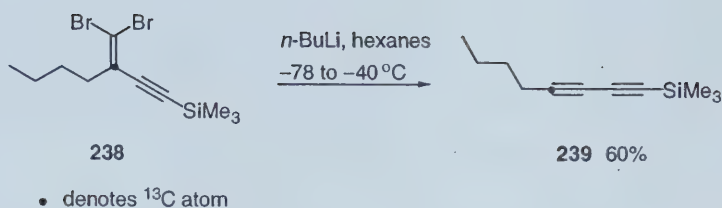
Preliminary studies carried out by Sara Eisler indicate that the intermediate is carbenoid in nature rather than a carbene,⁸ and this is in agreement with the literature.^{2,9} It has been reported that carbene formation is not observed during reactions where the FBW rearrangement occurs, and this is substantiated by the fact that products of typical carbene reactions, like addition onto multiple bonds and insertion reactions, have not been observed during these rearrangement processes.⁹ Furthermore, the rearrangement process has been reported to be stereospecific,^{10,11} further indicating that the intermediate is not a free carbene. Unlike the true FBW rearrangement which involves the migration of only a phenyl or aryl group, most of the rearrangements we have explored involve the possibility of a competition, for example between an alkynyl moiety and a phenyl, vinyl or alkyl group. Reported herein are the preliminary results of our efforts to determine the answers to the remaining three questions with respect to alkyne migration.

4.2. Results and Discussion

4.2.1. ¹³C-labelling experiments

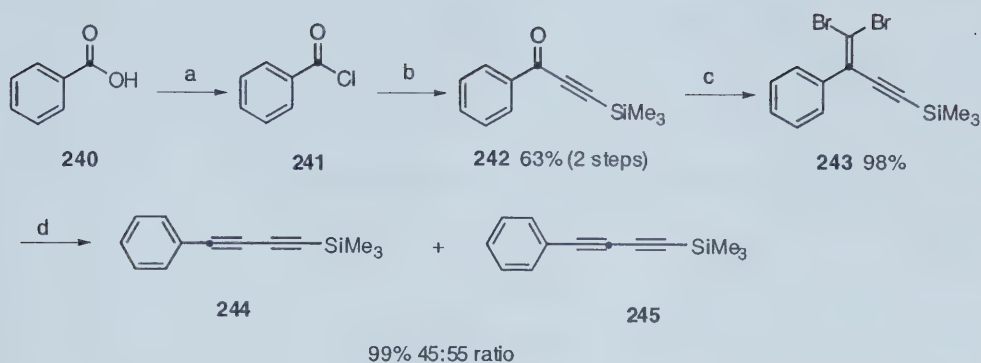
In order to determine which group migrates, ¹³C-labelling experiments were carried out for a variety of examples. In previous work, Sara Eisler has recently synthesized the ¹³C-labelled dibromoolefin **238** which, upon rearrangement using *n*-BuLi, gave only one product: diyne **239**, resulting from alkynyl migration, in 60% yield (Scheme 4.1).¹² No indication that the alkyl migrated was observed.¹² This is consistent with observations of others that alkyl groups make poor migrating groups in either carbene or carbenoid rearrangements.²

Scheme 4.1



^{13}C -labelling experiments were then carried out to investigate the migratory potential of the alkynyl moiety relative to a phenyl group. First, the rearrangement of dibromoolefin **243**, containing a trimethylsilyl-protected acetylene group and a phenyl unit, was studied (Scheme 4.2). The first step in the synthesis of dibromoolefin **243** involved formation of acid chloride **241** from commercially available benzoic- $\text{carboxy-}^{13}\text{C}$ acid (**240**) using thionyl chloride under reflux. Then, Friedel–Crafts acylation of acid chloride **241** with bis(trimethylsilyl)acetylene produced ketone **242** in 63% yield (over 2 steps from the carboxylic acid). Subjecting compound **242** to Corey–Fuchs dibromoolefination conditions¹³ gave compound **243** in 98% yield. Rearrangement of dibromoolefin **243** afforded a 45:55 ratio of diynes **244** and **245** in a combined yield of 99%, thus indicating an almost equal propensity for migration by the phenyl and trimethylsilylacetylene groups in this reaction.

Scheme 4.2

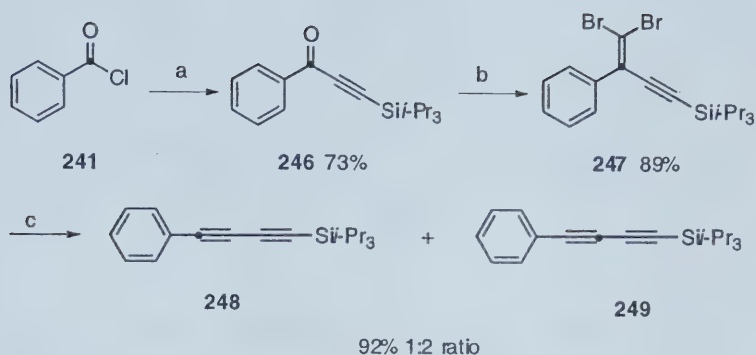


(a) SOCl_2 , reflux. (b) $\text{Me}_3\text{SiC}\equiv\text{CSiMe}_3$, AlCl_3 , CH_2Cl_2 , 0 to 25 °C. (c) PPh_3 (2 equiv), CBr_4 , rt. (d) $n\text{-BuLi}$, hexanes, -78 to -40 °C.

Investigation of the migratory competition between the alkynyl group and the aryl moiety was continued with a study of the rearrangement of dibromoolefin **247**, containing a triisopropylsilylacetylene group and a phenyl group (Scheme 4.3).¹⁴ Friedel–Crafts acylation of acid chloride **241** with (triisopropylsilyl)trimethylsilylacetylene yielded ketone **246** in 73% yield. Dibromoolefination of ketone **246** afforded compound **247** in 89% yield. Rearrangement of dibromoolefin **244** yielded a 1:2 mixture of diynes **248** and **249**, respectively, in a combined 92% yield. Thus, in this case, the amount of diyne resulting from migration of the phenyl group was two-fold greater relative to the diyne formed by migration of the triisopropylsilylacetylene moiety.

Upon comparison of the ratio of isomers obtained upon substituting the trimethylsilyl group with a triisopropylsilyl moiety which progresses from a 45:55 to a 1:2 ratio in favor of phenyl migration, questions about whether the migration is affected by steric effects arise. Thus far, however, no conclusion can be reached based on these two systems only and further experimentation is required.

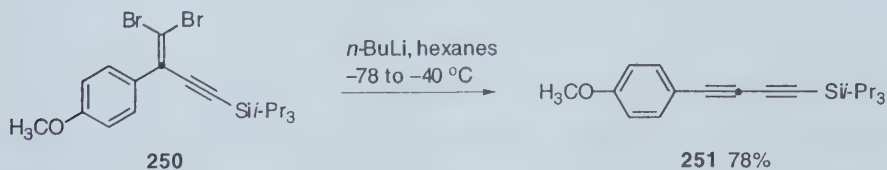
Scheme 4.3



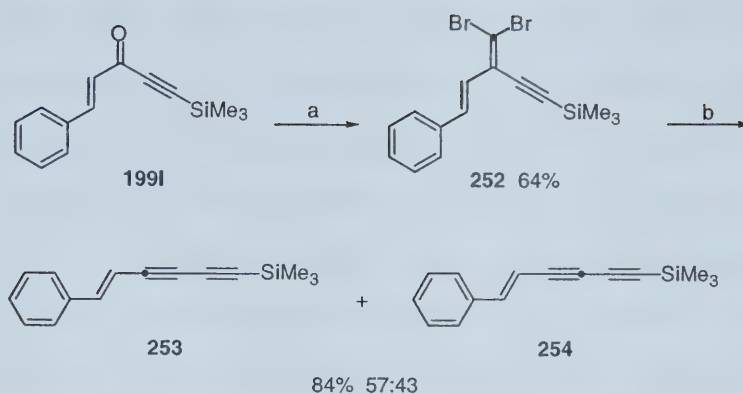
(a) $\text{Me}_3\text{SiC}\equiv\text{CSiMe}_3$, AlCl_3 , CH_2Cl_2 , 0 to 25 °C. (b) PPh_3 (2 equiv), CBr_4 , rt.
 (c) $n\text{-BuLi}$, hexanes, -78 to -40 °C.

In a related study, Erin Chernick in our group investigated the rearrangement of ^{13}C -labelled dibromoolefin **250** under similar conditions (Scheme 4.4).¹⁵ The sole product obtained from this rearrangement process was diyne **251** (78% yield), indicating that the anisyl group underwent preferential migration over the alkynyl functionality. It has previously been shown that the anisyl moiety migrates preferentially over a phenyl group.¹⁶ The results obtained here are consistent with this observation considering the 1:2 ratio in favor of phenyl migration in the previous case compared to sole migration by the anisyl group to the detriment of the alkynyl moiety in this instance. However, no conclusion can be reached until further experimentation is performed, due to the outstanding question of the lithiation process (*vide infra*).

Scheme 4.4

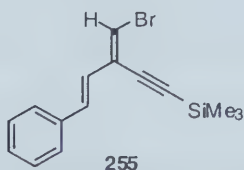


Scheme 4.5



(a) PPh_3 (2 equiv), $^{13}\text{CBr}_4$, rt. (b) $n\text{-BuLi}$, hexanes, -78 to -40 °C.

The migratory competition between the alkynyl group relative to a vinyl moiety has also been investigated (Scheme 4.5). ^{13}C -labelled dibromoolefin **252** was synthesized via the reaction of ketone **199I**¹⁷ with ^{13}C -labelled carbon tetrabromide and triphenylphosphine under Corey–Fuchs conditions¹³ in 64% yield. Rearrangement of dibromoolefin **252** afforded, under optimized conditions, a 57:43 ratio of diynes **253** and **254** in 89% yield, indicative of a slightly greater preference for vinyl migration over alkynyl migration. Interestingly, the results obtained for this rearrangement process were dependent upon the temperature at which the reaction was conducted. When the reaction



temperature was maintained at -78 °C, the reaction failed to go to completion, and unreacted dibromoolefin **252** was recovered, as well as monobromoolefin **255**,¹⁸ obtained as a result of protonation of the carbenoid species upon workup. The diynes **253** and **254** were isolated in a 17:83 ratio in an overall 22% combined yield. When the reaction

was repeated and the temperature was allowed to gradually increase from $-78\text{ }^{\circ}\text{C}$ to $-40\text{ }^{\circ}\text{C}$, all of the dibromoolefin **252** reacted, as monitored by TLC. In this case, monobromoolefin **255** was still isolated, along with a 47:53 ratio of diynes **253** and **254** in 54% combined yield. Upon forcing the reaction to completion by a combination of allowing the reaction mixture to warm up from $-78\text{ }^{\circ}\text{C}$ to $-40\text{ }^{\circ}\text{C}$ and using an excess of *n*-BuLi, diynes **253** and **254** were obtained in a 57:43 ratio in 84% combined yield. These results suggest that the ratio of products is dependent upon the progress of the reaction. It is worth noting that as the reaction goes further to completion, the ratio of the diyne resulting from alkynyl migration (**254**) steadily decreases until the diyne resulting from vinyl migration (**253**) becomes the major product. Thus, the ratio of **253** and **254** and the presence of **255** raise the question of whether the alkynyl moiety migrates faster than the vinyl group.

4.2.2. ^{13}C NMR spectral data of selected diynes

Herein is a discussion of the ^{13}C NMR spectral data used to identify the diyne products, their respective ratios, and consequently the migrating groups. In the case of diynes **244** and **245**, the ^{13}C NMR spectrum (Figure 4.1) revealed the presence of both isomers on account of two intense signals at δ 76.6 and 74.1 corresponding to ^{13}C -labelled atoms C5 and C6, respectively (Figure 4.2). Integration of these two peaks showed a 45:55 ratio. The ^{13}C NMR spectral data for the unlabelled parent diyne (**256**) of compounds **244** and **245** has previously been reported by Brandsma and coworkers¹⁹ as shown in Table 4.1 (Entry 1). Based on the coupling patterns observed in the ^{13}C NMR spectrum, we have been able to assign the signals to compounds **244** and **245**, respectively, as summarized in Table 1 and Figure 4.2. As will become apparent, a discrepancy in the carbon atom assignment of **256**, as previously published, has been found, and it involves the chemical shift values at δ 90.6 and 87.8 assigned by the

authors to C7 and C8, respectively.¹⁹ In the spectrum of **244** and **245**, two doublets at δ 87.8 with coupling constants of 148 (C7 for **245**) and 18 (C7 for **244**) Hz, corresponding to $^1J_{CC}$ and $^2J_{CC}$ values, respectively. A single doublet is seen at δ 90.6 with a coupling constant of 14 Hz, consistent with $^2J_{CC}$ or $^3J_{CC}$ coupling, which is the degenerate signal of C8 for both **244** and **245**. This observed pattern indicates that the resonance at δ 87.8 should correspond to C7, and δ 90.6 is attributable to C8. An interesting feature in the ^{13}C NMR spectrum is the presence of an AB quartet centered at δ 75.2.²⁰ This results from coupling between ^{13}C -labelled C5 atom and the natural abundance of ^{13}C at C6 of diyne **244** and from coupling between ^{13}C -labelled C6 and the natural abundance of ^{13}C at C5 of its isomer **245**.

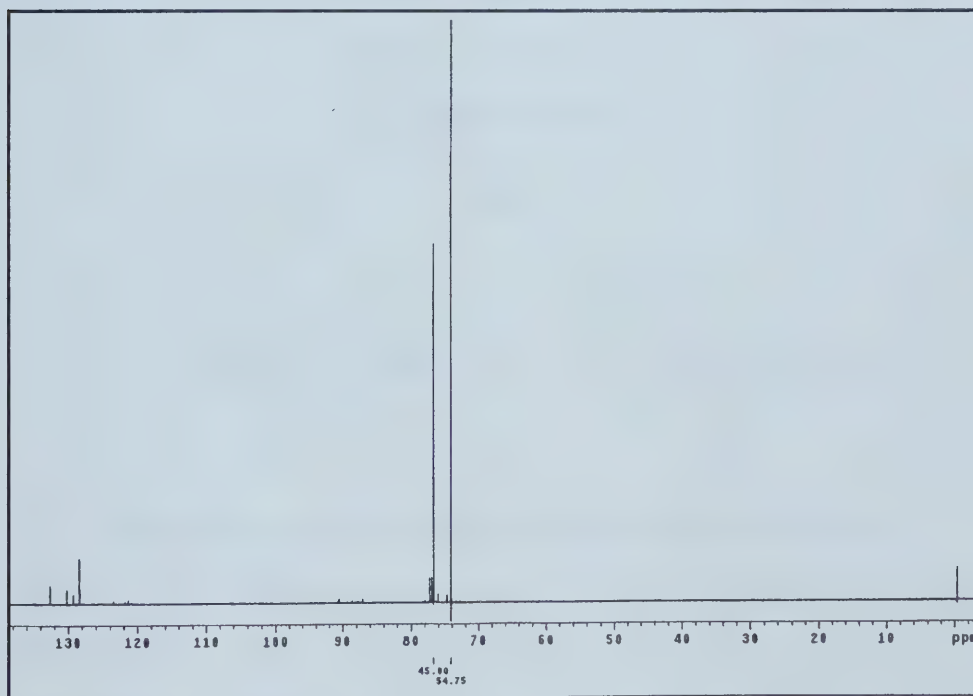


Figure 4.1. ^{13}C NMR spectrum for diynes **244** and **245**.

Table 4.1. ^{13}C NMR data for diynes **244**, **245** and **256** in CDCl_3 at rt.^{a,b}

Compd	C1	C2	C3	C4	C5	C6	C7	C8
256	121.2	132.5	128.3	129.2	76.6	74.3	[90.3]	[88.0]
244	121.4 (d, 92 Hz)	132.6 (d, 3 Hz)	128.4 (d, 6 Hz)	129.3 (d, 1 Hz)	76.1	74.1 ^c (196 Hz)	87.8 (d, 18 Hz)	90.6 (d, 14 Hz)
245	121.4 (d, 14 Hz)	132.6 (d, 2 Hz)	128.4 (s)	129.3	76.1 ^c (196 Hz)	74.1	87.8 (d, 148 Hz)	90.6 (d, 14 Hz)

^aThe carbon atom assignment for compound **256** is listed as reported in the literature (ref. 19) and contains a discrepancy (shown in brackets) which is discussed in the text.

^bThe chemical shift values are in ppm, and the multiplicity and the J values are shown in parentheses.

^cOne half of an AB quartet resulting from coupling between ^{13}C -labelled C5 atom and the natural abundance of ^{13}C at C6 of diyne **244** and from coupling between ^{13}C -labelled C6 and the natural abundance of ^{13}C at C5 of its isomer **245**.

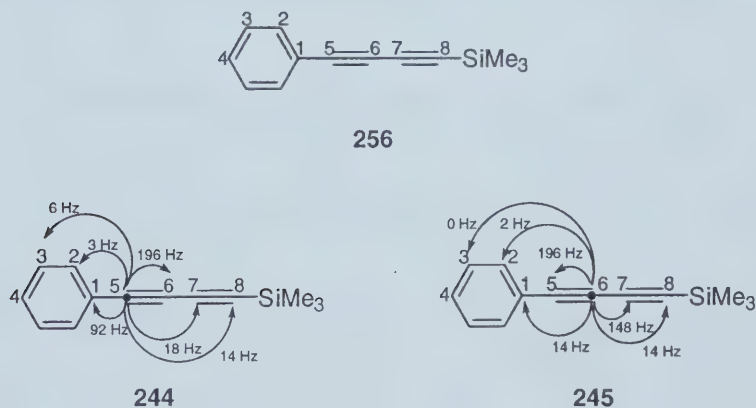


Figure 4.2. Coupling constants for diynes **244**, **245** and **256**.

Similarly, the ^{13}C NMR spectrum for diynes **248** and **249** showed the presence of both isomers in a 1:2 ratio based on the integration of the two intense signals at δ 75.5 and δ 74.6 which correspond to ^{13}C -labelled C7 and C8, respectively (Figure 4.3). A nearly identical coupling pattern as in the case of **244** and **245** is observed, including an AB quartet for C5 and C6.²⁰ Details of this analysis, as well as values for unlabelled diyne **257**, are summarized in Table 4.2 and Figure 4.4.

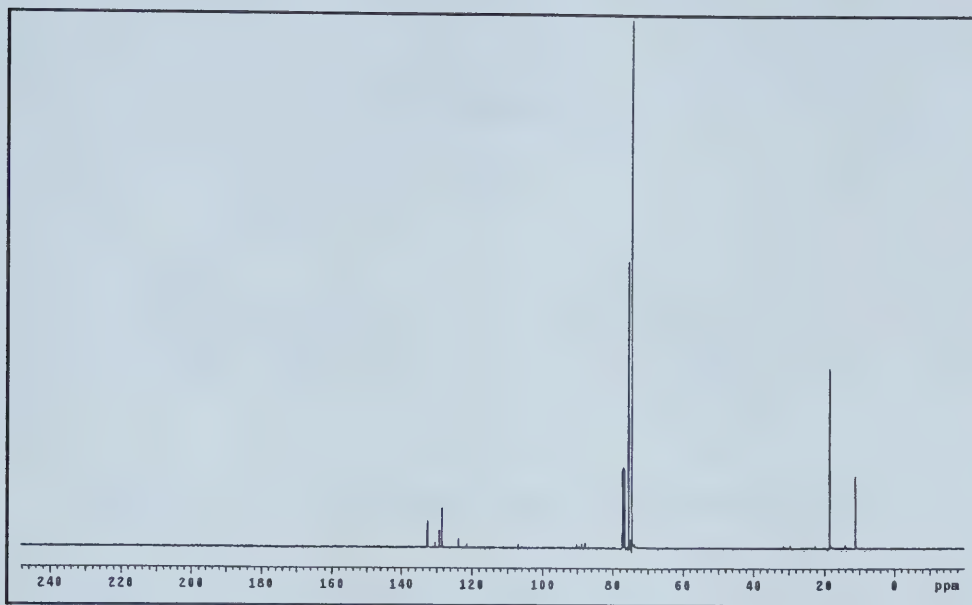


Figure 4.3. ^{13}C NMR spectrum for diynes **248** and **249**.

Table 4.2. ^{13}C NMR data for diynes **248**, **249** and **257** in CDCl_3 at rt.^a

Compd	C1	C2	C3	C4	C5	C6	C7	C8
257	121.6	132.7	128.2	129.2	75.6	74.7	89.5	87.9
248	121.5 (d, 95 Hz)	132.6 (d, 3 Hz)	128.3 (d, 6 Hz)	129.2 (d, 1 Hz)	75.5	74.6 ^b (207 Hz)	89.5 (d, 17 Hz)	87.8 (d, 14 Hz)
249	121.5 (d, 14 Hz)	132.6 (d, 2 Hz)	128.3	129.2	75.5 ^b (207 Hz)	74.6	89.5 (d, 147 Hz)	87.8 (d, 14 Hz)

^aThe chemical shift values are in ppm, and the multiplicity and J values are shown in parentheses.

^bOne half of an AB quartet resulting from coupling between ^{13}C -labelled C5 atom and the natural abundance of ^{13}C at C6 of diyne **248** and from coupling between ^{13}C -labelled C6 and the natural abundance of ^{13}C at C5 of its isomer **249**.

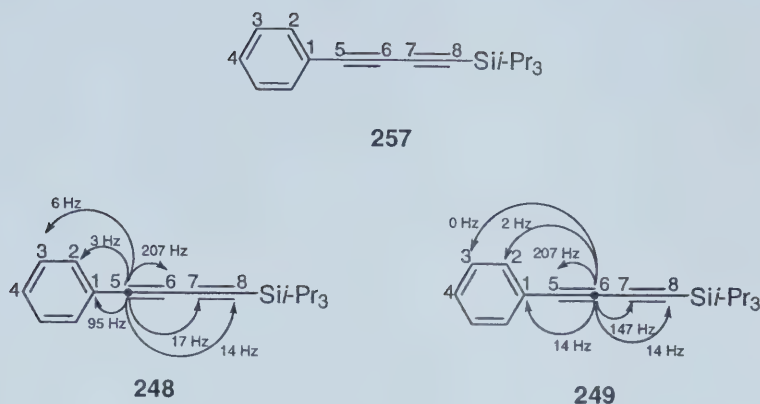


Figure 4.4. Coupling constants for diynes **248**, **249** and **257**.

^{13}C NMR analysis provides information about the connectivity in diynes **253** and **254**. The two intense signals at δ 76.5 and 76.3, corresponding to ^{13}C -labelled C7 and C8, respectively, show a 57:43 ratio (Figure 4.5). An AB quartet, similar to the aforementioned cases, is also observed.¹⁸ This results from coupling between ^{13}C -labelled C7 atom and natural abundance of ^{13}C at C8 of diyne **253** and from coupling between ^{13}C -labelled C8 and natural abundance of ^{13}C at C7 of its isomer **254**. Details about the carbon atom assignments and the coupling pattern are summarized in Table 4.3 and Figure 4.6. A notable difference when comparing diynes **244** and **245** with diynes **253** and **254**, is the smaller $^1J_{\text{CC}}$ value (170 Hz) for C7–C8 of diynes **253** and **254** compared to the $^1J_{\text{CC}}$ value (196 Hz) for C5–C6 of diynes **244** and **245**. This smaller value may be attributable to a change in bond order, since there is an increase in conjugation with the additional vinyl group in the system.

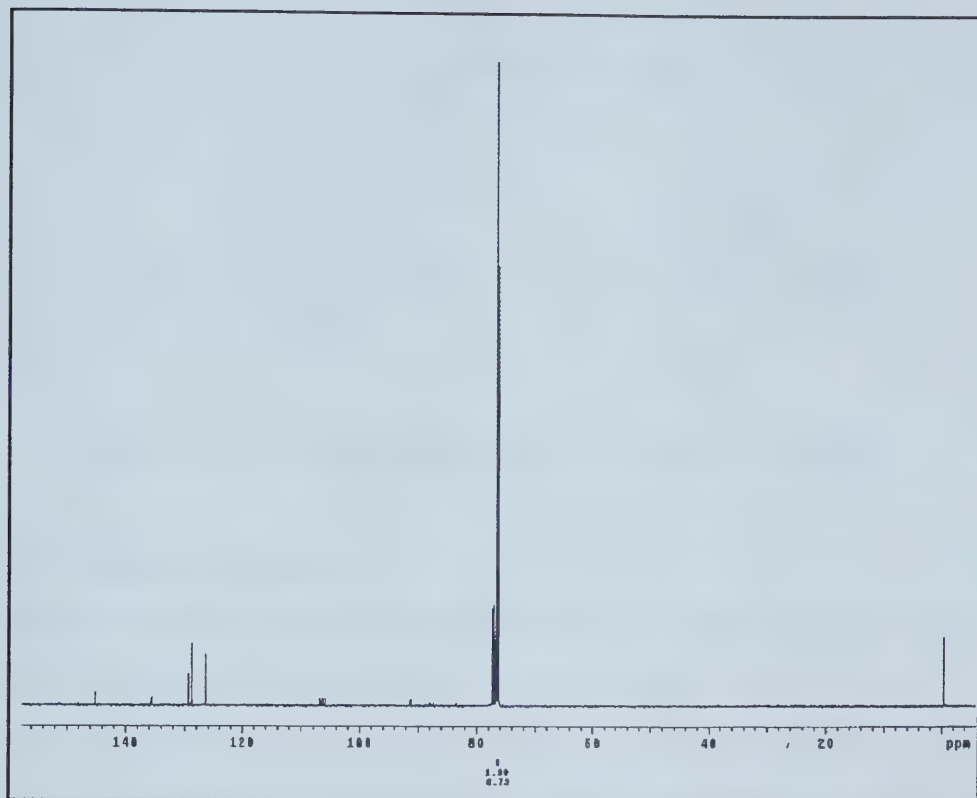


Figure 4.5. ^{13}C NMR spectrum for diynes **253** and **254**.

Table 4.3. ^{13}C NMR data for diynes **2011**, **253** and **254** in CDCl_3 at rt.^a

Compd	C1	C5	C6	C7	C8	C9	C11
2011	135.6	145.1	106.3	76.5	76.3	88.0	91.3
253	135.6 (d, 9 Hz)	145.1 (d, 1 Hz)	106.3 (d, 93 Hz)	76.5	76.3 ^b (170 Hz)	88.0 (d, 18 Hz)	91.3 (d, 18 Hz)
254	135.6	145.1 (d, 5 Hz)	106.3 (d, 13 Hz)	76.5 ^b (170 Hz)	76.3	88.0 (d, 148 Hz)	91.3 (d, 14 Hz)

^aThe chemical shift values are in ppm, and the multiplicity and J values are shown in parentheses.

^bOne half of an AB quartet resulting from coupling between ^{13}C -labelled C7 atom and the natural abundance of ^{13}C at C8 of diyne **253** and from coupling between ^{13}C -labelled C8 and the natural abundance of ^{13}C at C7 of its isomer **254**.

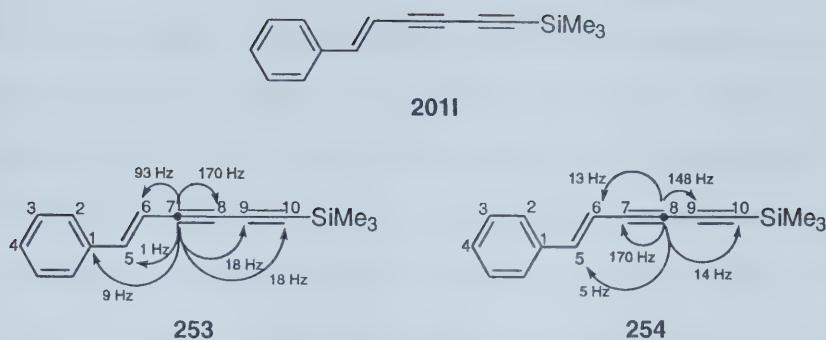


Figure 4.6. Coupling constants for diynes **2011**, **253** and **254**.

4.2.3. Trapping experiments

The next mechanistic aspect to be considered is the site of lithium-halogen exchange, which would provide information about the regiospecificity of this process. To determine the site of lithiation, trapping of the carbenoid intermediate by protonation was planned. The structure of the resulting monobromoolefin(s) could then be elucidated by 2D-NMR spectroscopic studies, and would indicate where lithiation had occurred (i.e. **255** vs. **258**). This, in turn, might suggest how the lithiation influenced the formation of the diynes produced in the rearrangement process. In addition, it might also shed light on the stereospecificity of the rearrangement, i.e. whether the migration occurs *cis* or *trans* to the halogen in the carbenoid intermediate, or a combination of both pathways. Elegant studies by Bothner-By and Curtin suggested *trans* migration relative to the bromine,¹¹ as depicted in Figure 4.7.²¹ The role of alkynes in the stereochemistry of the migration is, however, unknown.



Figure 4.7. Migration of group *trans* to bromine atom.

As mentioned earlier, monobromoolefin **255** was isolated from the rearrangement reaction of compound **252**. NOE studies, namely GOESY experiments, conducted on this compound revealed a through space interaction between the proton of the vinyl bromide moiety (δ 6.70, d, $J_{\text{CH}} = 196$ Hz) and the closest vinylic proton (δ 6.67, dd, $J = 15.7, 5.4$ Hz) from the styryl moiety (Figure 4.8). This is demonstrated in Figure 4.8, where irradiation at δ 6.67 shows an enhancement of the two signals of the doublet at δ 6.52 and 6.92. This suggests that the monobromoolefin isolated has the structure **255** since the distance calculated between the two protons (Figure 4.9), using MacSpartan computer modeling program,²² was found to be 2.5 Å which allows for NOE interaction. This analysis, however, cannot conclusively rule out the other isomeric structure **258**, as the distance between the two protons is 3.8 Å, and this is also within possible distance for NOE interaction.

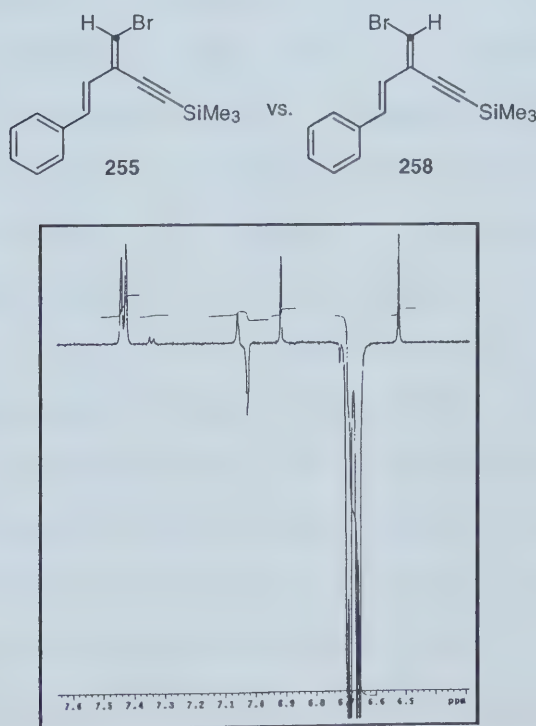


Figure 4.8. GOESY spectrum for monobromoolefin **255** (irradiation at δ 6.67).

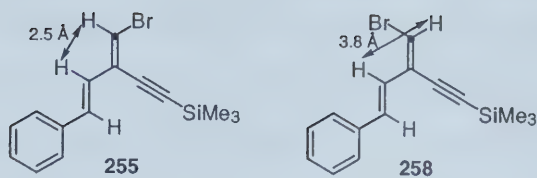
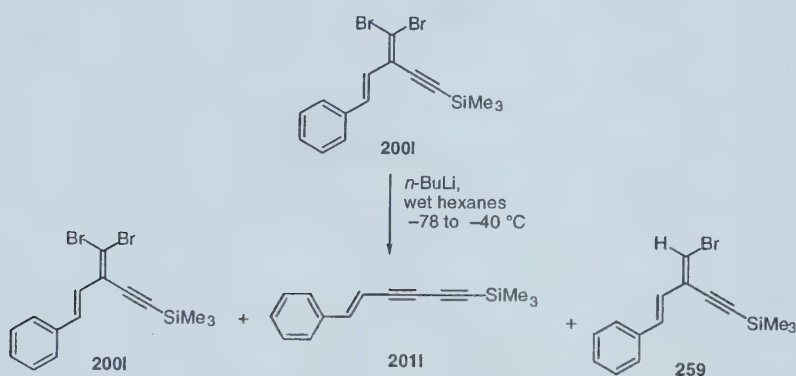


Figure 4.9. Calculated bond lengths for compounds 255 and 258.

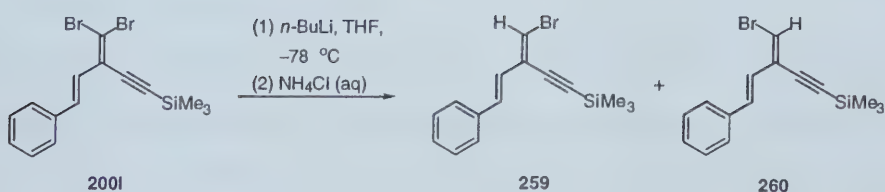
Trapping experiments were then performed on the corresponding unlabelled dibromoolefin **200l**. Several different conditions for trapping the carbenoid intermediate were explored. First, use of dry hexanes as the solvent was substituted with wet hexanes with the other conditions unaltered, and this produced a mixture of unreacted dibromoolefin **200l**, rearranged product (diyne **201l**) and a single monobromoolefinic product (Scheme 4.6). This product had similar R_f value and ^1H NMR spectral data as the ^{13}C -labelled congener **255**, suggesting the structure **259**. This general approach, however, did not give reproducible results: in some cases, the reaction would give only diyne **201l** without any monobromoolefin. Thus, optimized trapping conditions involved using dry THF instead of hexanes and quenching the reaction with sat. aq. NH_4Cl within minutes of addition of $n\text{-BuLi}$ at -78°C (Scheme 4.7). This resulted reproducibly in a binary mixture of monobromoolefin isomers (**259** and **260**) as shown by TLC and ^1H NMR spectroscopy. Analysis of the ^1H NMR spectrum showed that the isomers occurred in a nearly equal ratio (44:56), with the more abundant monobromoolefin being **259**. In addition to establishing the similar nature of the ^1H NMR data and R_f value of **259** to that of the ^{13}C -labelled monobromoolefin **255**, the structural assignment of **259** is based on TROESY analysis as shown in Figure 4.10. Clearly evident are correlations between the signal for the proton of the vinyl bromide moiety at δ 6.71 and that of the doublet for the vinyl proton of the styryl moiety at δ 6.67. Considering that the diynes **253** and **255** were produced in a 57:43 ratio, there appears to be a correlation between

site of lithiation and rearrangement products, suggesting a *trans* migration relative to the bromine atom. No conclusion, however, can be made until further experimentation is performed and the effect of changing the solvent to THF is determined. Furthermore, the structure of the monobromoolefins **259** and **260** need to be more rigorously established. X-ray crystallographic analysis of the monobromoolefins would be extremely informative, but so far the monobromoolefins isolated have been intractable to forming suitable crystals.

Scheme 4.6



Scheme 4.7



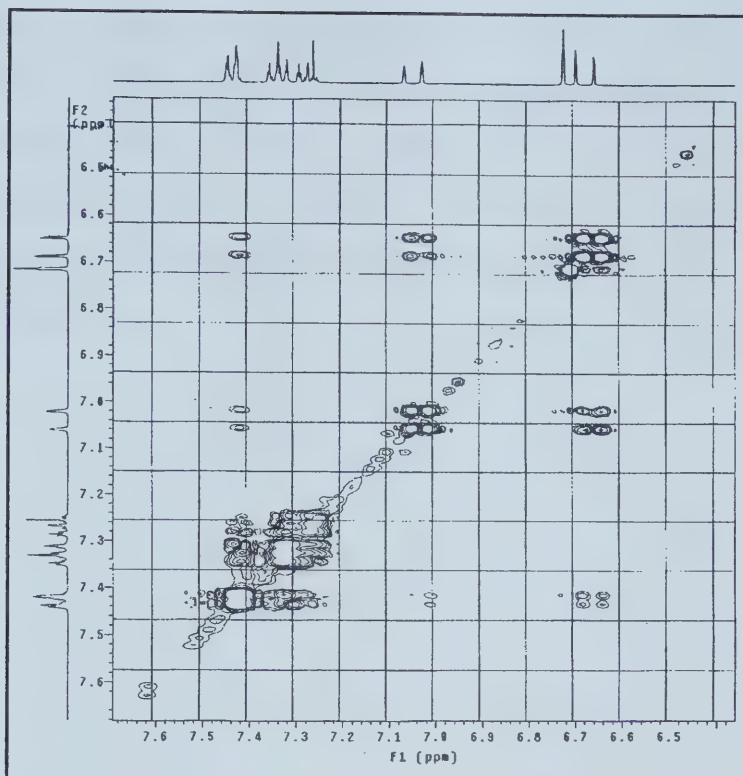


Figure 4.10. TROESY spectrum for monobromoolefin 259.

4.3. Conclusions and Prospects

In summary, ^{13}C -labelling experiments have been performed to investigate the mechanism of the modified FBW rearrangement. A comparison of the competition of the alkynyl moiety relative to alkyl, aryl and vinyl functionalities has been carried out. Thus, the alkynyl group is more likely to migrate than an alkyl chain. In turn, aryl groups seem to migrate preferentially to alkynyl groups, but the extent of this preference is dependent upon the system studied. As a result, no definite conclusion can be made until further experimentation.

Preliminary results from trapping experiments suggest that, in the rearrangement process, it is the group *trans* to the bromine atom that migrates but again no definitive conclusion can be reached. Future experiments include further trapping experiments, structure elucidation through 1D and 2D NMR analysis, and X-ray crystallographic studies. Furthermore, it would also be desirable to lithiate the monobromoolefins using LDA to demonstrate that these species are capable of rearrangement, stereospecifically, to the corresponding diyne.

4.4. References

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(14) Work carried out by summer undergraduate student, Paul Bichler, under my supervision.

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- (20) An expansion of the AB quartet is shown in Appendix B.
- (21) The stereochemical integrity of the intermediate vinylolithium species is known to be preserved, see ref. 2e.
- (22) MACSPARTAN *Plus* version 1.1.9.

Chapter 5. Experimental

General. Reagents were purchased reagent grade from commercial suppliers and used without further purification. Et₂O, THF and benzene were distilled from sodium/benzophenone ketyl, and hexanes, acetonitrile and dichloromethane were distilled from CaH₂ immediately prior to use. Anhydrous MgSO₄ or Na₂SO₄ were used as the drying agent after aqueous work-up. Evaporation and concentration *in vacuo* was done at H₂O-aspirator pressure. All reactions were performed in standard, dry glassware under an inert atmosphere of N₂. Column chromatography: *silica gel-60* (230-400 mesh) from *General Intermediates of Canada*. Thin Layer Chromatography (TLC): plastic sheets covered with *silica gel-60 F₂₅₄* from *Macherey-Nagel*; visualization by UV light or KMnO₄ stain. Mp: *Gallenkamp* apparatus; uncorrected. IR spectra (cm⁻¹): *Nicolet Magna-IR 750* (neat) or *Nic-Plan IR Microscope* (solids). ¹H- and ¹³C-NMR: *Varian Gemini-300*, *400* or *500* and *Bruker AM-300* or *400* instruments, at rt in CD₂Cl₂, CDCl₃, C₆D₆ or CD₃CN; solvent peaks (5.32, 7.24, 7.15 and 1.96 ppm, respectively, for ¹H and 53.8, 77.0, 128.6 and 1.8 ppm, respectively, for ¹³C) as reference. EI MS (*m/z*): *Kratos MS50* instrument. Elemental analyses were effected by Spectral Services at the University of Alberta.

Compounds **S1–S3** that served as starting materials are also reported here, but do not have compound numbers in the text.

For simplicity, the coupling constants of the aryl protons for *para*-substituted phenyl groups have been reported as pseudo first-order, even though they are second-order spin systems. For mass spectral analyses, low-resolution data are provided in cases when M⁺ is not the base peak; otherwise, only high-resolution data are provided.

General Procedure for Alcohol Formation. To trimethylsilylacetylene (1.23 g, 12.5 mmol, 1.25 equiv) in Et₂O (50 mL) at –78 °C was added *n*-BuLi (2.5 M in hexanes, 4.8 mL, 12 mmol, 1.2 equiv). After stirring for 30 min, the appropriate aldehyde (10 mmol, 1 equiv) in Et₂O (5 mL) was added. The reaction mixture was slowly warmed to ca. –10 °C until the reaction was judged complete by TLC analysis. The reaction

was quenched with satd. aq. NH_4Cl at $-78\text{ }^\circ\text{C}$, the organic layer washed with brine ($2 \times 50\text{ mL}$), and dried (MgSO_4). The resulting alcohol could generally be used without further purification.

General Procedure for Ketone Formation via Oxidation using PCC. To the appropriate alcohol (4 mmol) in CH_2Cl_2 (50 mL) was added sequentially Celite (equal amount by mass to PCC), molecular sieves ($4\text{ \AA}$, equal amount by mass to PCC), and PCC (5 mmol, 1.25 equiv). After stirring at rt until the reaction was judged complete by TLC analysis, the solution was filtered through a plug of silica (CH_2Cl_2) and the solvent was evaporated to give the corresponding ketone. The ketone was of sufficient purity to be carried on directly to the dibromoolefination step without further purification or it could be isolated pure by column chromatography.

General Procedure for Ketone Formation via Oxidation using BaMnO_4 . To the appropriate alcohol (4 mmol) in CH_2Cl_2 (50 mL) was added barium manganate (3 equiv). After stirring at rt until the reaction was judged complete by TLC analysis, the solution mixture was filtered through a pad of Celite. The solvent was evaporated to give the corresponding ketone.

General Procedure for Ketone Formation via Friedel–Crafts Acylation. The formation of **202a–f**, **205a–f**, **218**, **221**, **224**, **226**, and **228** was accomplished as reported for similar derivatives.* Commercially available acid chlorides were used except for 4-phenylazobenzoyl chloride, 3-(2-thienyl)acryloyl chloride, sorbyl chloride, 3-(2-furyl)acryloyl chloride, and phenylpropiolyl chloride which were made from the corresponding carboxylic acids. *See: (a) Walton, D. R. M.; Waugh, F. J. *Organomet. Chem.* **1972**, 37, 45–56. (b) Suzuki, R.; Tsukuda, H.; Watanabe, N.; Kuwatani, Y.; Ueda, I. *Tetrahedron* **1998**, 54, 2477–2496.

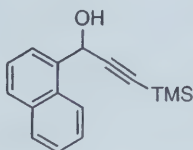
General Procedure for Acid Chloride Formation. To the appropriate carboxylic acid (1 equiv) was added thionyl chloride (6 equiv). After stirring for 24 hours, the

excess thionyl chloride was evaporated, and the acid chloride was used directly in the next step without further purification.

General Procedure for Dibromoolefin Formation. Literature procedures were followed as referenced. In some cases, and to date unexplained, reactions conducted under reported conditions would fail to go to completion using the normal amounts of PPh_3 and CBr_4 . In these cases, an additional equivalent of both PPh_3 and CBr_4 would be added in order to force the reaction to completion.

General Procedure for Diyne formation. Unless otherwise noted, the following procedure was followed. To the appropriate dibromoolefin (0.368 mmol) in dry hexanes (10 mL) at $-78\text{ }^\circ\text{C}$ was added dropwise over ten minutes 1.1-1.2 equivalent of $n\text{-BuLi}$ (0.15 mL, 2.5 M in hexanes, 0.38 mmol). The mixture was warmed to approximately $-40\text{ }^\circ\text{C}$ for 30 min, re-cooled to $-78\text{ }^\circ\text{C}$, and quenched with a saturated aqueous solution of NH_4Cl . Et_2O was added ($\sim 50\text{ mL}$), the organic layer separated, washed with a saturated aqueous solution NH_4Cl , and dried over magnesium sulfate. Solvent removal *in vacuo* and passing the residue through a short plug of silica gel with the solvent system detailed for each product afforded the desired diyne. If necessary, additional purification could be achieved via flash column chromatography.

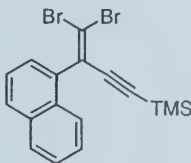
1-(1-Naphthyl)-3-trimethylsilylprop-2-yn-1-ol (198a).



To (trimethylsilyl)acetylene (0.945 g, 9.62 mmol) in diethyl ether (10 mL) at $-78\text{ }^\circ\text{C}$ was added $n\text{-BuLi}$ (3.8 mL, 2.5 M in hexanes, 9.5 mmol). After stirring for 0.5 h, 1-naphthaldehyde (1.5 g, 1.3 mL, 9.6 mmol) was added and the general procedure was followed to give **198a** (1.54 g, 64%) as a thick yellow oil: $R_f = 0.25$ (hexanes/ CH_2Cl_2 1:1); IR (CH_2Cl_2 cast) 3364, 3050, 2959, 2898, 2173, 1598, 1250 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.28 (d, $J = 8.4\text{ Hz}$, 1H), 7.85 (m, 3H), 7.51 (m, 3H), 6.11 (d, $J = 5.0$

Hz, 1H), 2.24 (d, $J = 5.0$ Hz, 1H), 0.20 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 135.3, 133.9, 130.6, 129.3, 128.6, 126.3, 125.8, 125.2, 124.7, 123.9, 104.7, 92.4, 63.3, -0.1 ; EI HRMS m/z calcd for $\text{C}_{16}\text{H}_{18}\text{OSi}$ (M^+) 254.1127, found 254.1126.

[4,4-Dibromo-3-(1-naphthyl)-buten-1-ynyl]trimethylsilane (200a).



To **198a** (1.41 g, 5.52 mmol) in CH_2Cl_2 (60 mL) were sequentially added Celite (2 g), molecular sieves ($4\text{\AA}$, 2 g), and PCC (1.99 g, 9.03 mmol) as per the general procedure to give ketone **199a** that, following workup, was subjected to dibromoolefination using CBr_4 (2.48 g, 7.36 mmol) and PPh_3 (3.87 g, 14.7 mmol) in CH_2Cl_2 (75 mL) to give **200a** (0.984 g, 44%) as a yellow oil: $R_f = 0.83$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 3058, 2959, 2897, 2141, 1593, 1507 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.99 (d, $J = 8.0$ Hz, 1H), 7.89 (m, 2H), 7.52 (m, 4H), 0.21 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 135.7, 133.6, 129.9, 129.8, 128.9, 128.3, 126.5, 126.3, 126.1, 125.3, 125.0, 104.8, 102.81, 102.80, -0.2 ; MS (EI, 70 eV) m/z 405.9/407.9/409.9 (M^+ , 18/36/19); HRMS m/z calcd for $\text{C}_{17}\text{H}_{16}\text{Si}^{79}\text{Br}_2/\text{C}_{17}\text{H}_{16}\text{Si}^{79}\text{Br}^{81}\text{Br}/\text{C}_{17}\text{H}_{16}\text{Si}^{81}\text{Br}_2$ (M^+) 405.9388/407.9368/409.9347, found 405.9396/407.9375/409.9357.

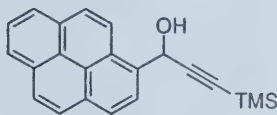
[4-(1-Naphthyl)-1,3-butadiynyl]trimethylsilane (201a).



Dibromoolefin **200a** (757 mg, 1.85 mmol) was reacted with $n\text{-BuLi}$ (1.0 mL, 2.5 M in hexanes, 2.5 mmol) as per the general procedure to give diyne **201a** (430 mg, 93%) as a yellow oil: $R_f = 0.3$ (hexanes); IR (CH_2Cl_2 cast) 3058, 2959, 2199, 2098, 1585, 1505 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.31 (d, $J = 8.1$ Hz, 1H), 7.86 (d, $J = 7.8$ Hz, 1H), 7.83 (d, $J = 8.1$ Hz, 1H), 7.73 (dd, $J = 7.2, 1.1$ Hz, 1H), 7.57 (ddd, $J = 8.3, 6.8, 1.4$ Hz, 1H), 7.51 (ddd, $J = 8.1, 6.8, 1.4$ Hz, 1H), 7.40 (dd, $J = 8.3, 7.2$ Hz, 1H), 0.27

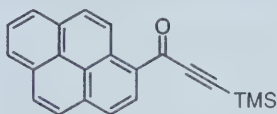
(s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 134.0, 133.0, 132.2, 129.7, 128.3, 127.1, 126.6, 126.0, 125.1, 119.0, 91.7, 88.0, 78.8, 75.1, -0.2; EI HRMS m/z calcd for $\text{C}_{17}\text{H}_{16}\text{Si}$ (M^+) 248.1021, found 248.1019.

1-(1-Pyrenyl)-3-trimethylsilylprop-2-yn-1-ol (**198b**).



To (trimethylsilyl)acetylene (1.30 g, 14.0 mmol) in diethyl ether (30 mL) at -78°C was added $n\text{-BuLi}$ (5.7 mL, 2.4 M in hexanes, 13.7 mmol). After stirring for 0.5 h, 1-pyrene carboxaldehyde (2.50 g, 10.9 mmol) was added and the general procedure was followed to give **198b** (3.43 g, 96%) as a light yellow solid: mp $100\text{--}101^\circ\text{C}$; $R_f = 0.3$ (hexanes/ CH_2Cl_2 1:1); IR (CHCl_3 cast) 3380, 3040, 2958, 2171, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.51 (d, $J = 9.3$ Hz, 1H), 8.36 (d, $J = 7.9$ Hz, 1H), 8.16 (m, 4H), 8.04 (m, 3H), 6.40 (d, $J = 5.7$ Hz, 1H), 2.37 (d, $J = 5.7$ Hz, 1H), 0.20 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 132.9, 131.7, 131.2, 130.7, 128.4, 127.9, 127.8, 127.3, 126.0, 125.5, 125.4, 125.1, 124.74, 124.70, 123.1, 105.1, 92.7, 63.4, -0.1 (one coincident signal not observed); MS (EI, 70 eV) m/z 328.1 (M^+ , 73), 73.0 ($[\text{Me}_3\text{Si}]^+$, 100); HRMS m/z calcd for $\text{C}_{22}\text{H}_{20}\text{OSi}$ (M^+) 328.1284, found 328.1276.

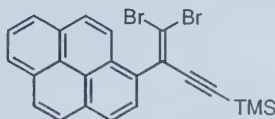
1-(1-Pyrenyl)-3-trimethylsilylpropynone (**199b**).



To **198b** (49.4 mg, 0.15 mmol) in CH_2Cl_2 (10 mL) were sequentially added Celite (40 mg), molecular sieves ($4\text{\AA}$, 40 mg), and PCC (39.7 mg, 0.18 mmol) as per the general procedure to give the ketone **199b** (40.9 mg, 83%) as a bright yellow solid: mp $111\text{--}112^\circ\text{C}$; $R_f = 0.62$ (hexanes/ Et_2O 7:3); IR (CHCl_3 cast) 2958, 2921, 2120, 1633, 1620, 1592 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.47 (d, $J = 9.4$ Hz, 1H), 8.92 (d, $J = 8.1$ Hz, 1H), 8.24 (m, 3H), 8.17 (d, $J = 8.7$ Hz, 2H), 8.04 (m, 2H), 0.20 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 179.6, 135.3, 131.8, 130.98, 130.95, 130.8, 130.6,

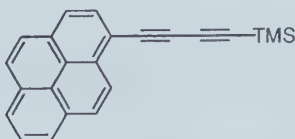
130.4, 128.8, 127.1, 127.0, 126.7, 126.5, 124.9, 124.7, 124.0, 103.1, 99.4, -0.5; EI HRMS m/z calcd for $C_{22}H_{18}OSi$ (M^+) 326.1127, found 326.1119.

[4,4-Dibromo-3-(1-pyrenyl)-buten-1-ynyl]trimethylsilane (200b).



To **198b** (1.64 g, 5.00 mmol) in CH_2Cl_2 (60 mL) were sequentially added Celite (1.5 g), molecular sieves (4Å, 1.5 g), and PCC (1.38 g, 6.25 mmol) as per the general procedure to give ketone **199b** that, following workup, was subjected to dibromoolefination using CBr_4 (2.07 g, 6.25 mmol) and PPh_3 (3.28 g, 12.5 mmol) in CH_2Cl_2 (75 mL) to give **200b** (0.923 g, 39%) as a brown solid: mp 137-139 °C; R_f = 0.7 (CH_2Cl_2); IR ($CHCl_3$ cast) 3046, 2958, 2134, 1249 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 8.23 (m, 5H), 8.06 (m, 4H), 0.27 (s, 9H); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 132.9, 131.5, 131.1, 130.9, 130.5, 128.2, 128.1, 127.9, 127.2, 126.2, 126.2, 125.5, 125.5, 124.9, 124.6, 124.4, 105.5, 103.3, 103.1, -0.3 (one coincident signal not observed); MS (EI, 70 eV) m/z 480.0/482.0/484.0 (M^+ , 19/42/23); HRMS m/z calcd for $C_{23}H_{18}OSi^{79}Br_2/C_{23}H_{18}OSi^{79}Br^{81}Br$ / $C_{23}H_{18}OSi^{81}Br_2$ (M^+) 479.9544/481.9524/483.9504, found 479.9604/481.9585/483.9558.

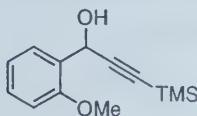
[4-(1-Pyrenyl)-1,3-butadiynyl]trimethylsilane (201b).



Dibromoolefin **200b** (177 mg, 0.367 mmol) was reacted in hexanes (20 mL) at -50 °C (rather than -78 °C due to decreased solubility of dibromoolefin **200b**) with *n*-BuLi (0.16 mL, 2.5 M in hexanes, 0.40 mmol) to give **201b** (92.8 mg, 79%) as a bright yellow solid: mp 124-125 °C; R_f = 0.8 (CH_2Cl_2 /hexanes 1:1); IR ($CHCl_3$ cast) 3046, 2195, 2095, 1250 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, J = 9.0 Hz, 1H), 8.10 (m, 4H), 7.98 (m, 3H), 7.92 (t, J = 9.0 Hz, 1H), 0.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.5, 131.8, 131.0, 130.8, 130.6, 128.8, 128.7, 127.0, 126.3, 125.9, 125.8,

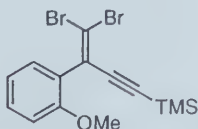
125.1, 124.3, 124.1, 123.9, 115.4, 92.2, 88.4, 79.6, 76.3, -0.2; EI HRMS m/z calcd for $C_{23}H_{18}Si$ (M^+) 322.1178, found 322.1174.

1-(2-Methoxyphenyl)-3-trimethylsilylprop-2-yn-1-ol (198c).*



To (trimethylsilyl)acetylene (1.08 g, 10.7 mmol) in diethyl ether (10 mL) at $-78\text{ }^{\circ}\text{C}$ was added n -BuLi (4.4 mL, 2.5 M in hexanes, 11.0 mmol). After stirring for 0.5 h, 2-methoxybenzaldehyde (1.50 g, 11.0 mmol) was added. Due to the insolubility of the aldehyde, the reaction mixture was allowed to warm to room temperature and stirred overnight. Workup as per the general procedure gave **198c** (2.33 g, 90%) as a pale yellow oil; R_f = 0.2 (hexanes/ CH_2Cl_2 1:1); IR (CH_2Cl_2 cast) 3426, 2959, 2900, 2838, 2172, 1601, 1590, 1491, 1464 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.57 (m, 1H), 7.29 (m, 1H), 6.97 (m, 1H), 6.89 (d, J = 8.3 Hz, 1H), 5.69 (d, J = 6.0 Hz, 1H), 3.87 (s, 3H), 2.90 (d, J = 6.0 Hz, 1H), 0.19 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 156.8, 129.6, 128.5, 127.9, 120.8, 110.8, 104.5, 90.9, 61.4, 55.6, -0.03; MS (EI, 70 eV) m/z 234.1 (M^+ , 62); HRMS m/z calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2\text{Si}$ (M^+) 234.1076, found 234.1070. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2\text{Si}$: C, 66.62; H, 7.74. Found C, 66.53; H, 7.86. *Previously reported by: Baldoli, C.; DelButtero, P.; Licandro, E.; Maiorana, S.; Papagni, A.; Torchio, M. *Tetrahedron Lett.* **1993**, 34, 7943-7946.

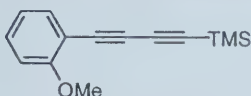
[4,4-Dibromo-3-(2-methoxyphenyl)-buten-1-ynyl]trimethylsilane (200c).



To **198c** (1.93 g, 8.25 mmol) in CH_2Cl_2 (80 mL) were sequentially added Celite (3 g), molecular sieves ($4\text{\AA}$, 3 g), and PCC (2.77 g, 12.7 mmol) as per the general procedure to give ketone **199c** that, following workup, was subjected to dibromoolefination using CBr_4 (3.53 g, 10.7 mmol) and PPh_3 (5.56 g, 21.3 mmol) in CH_2Cl_2 (100 mL) to give **200c** (1.91 g, 59%) as a yellow oil; R_f = 0.85 (CH_2Cl_2); IR (CH_2Cl_2 cast) 3003, 2959,

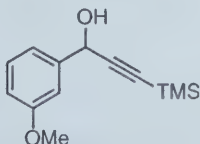
2898, 2835, 2149, 1597, 1582, 1542, 1489, 1462 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.33 (m, 1H), 7.19 (dd, $J = 5.7, 1.7$ Hz, 1H), 6.93 (dt, $J = 7.4, 1.1$ Hz, 1H), 6.90 (d, $J = 7.4$ Hz, 1H), 3.84 (s, 3H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 155.9, 130.0, 129.7, 127.9, 127.1, 120.5, 111.6, 102.9, 102.8, 102.2, 55.7, -0.2 ; MS (EI, 70 eV) m/z 385.9/387.9/389.9 (M^+ , 50/100/52); HRMS m/z calcd for $\text{C}_{14}\text{H}_{16}\text{OSi}^{79}\text{Br}_2/\text{C}_{14}\text{H}_{16}\text{OSi}^{79}\text{Br}^{81}\text{Br}/\text{C}_{14}\text{H}_{16}\text{OSi}^{81}\text{Br}_2$ (M^+) 385.9337/387.9317/389.9296, found 385.9342/387.9325/389.9309.

[4-(2-Methoxyphenyl)-1,3-butadiynyl]trimethylsilane (**201c**).



Dibromoolefin **200c** (82.0 mg, 0.211 mmol) was reacted with *n*-BuLi (0.10 mL, 2.5 M in hexanes, 0.25 mmol) as per the general procedure to give diyne **201c** (20.6 mg, 43%) as a yellow oil: $R_f = 0.7$ (hexanes/ CH_2Cl_2 1:1); IR (CH_2Cl_2 cast) 2959, 2836, 2204, 2103, 1594, 1273 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.43 (m, 1H), 7.30 (m, 1H), 6.86 (m, 2H), 3.86 (s, 3H), 0.21 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 161.6, 134.5, 130.7, 120.4, 110.6, 91.0, 88.1, 77.9, 73.3, 55.8, -0.2 (one coincident peak not observed); EI HRMS m/z calcd for $\text{C}_{14}\text{H}_{16}\text{OSi}$ (M^+) 228.0971, found 228.0967.

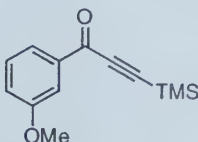
1-(3-Methoxyphenyl)-3-trimethylsilylprop-2-yn-1-ol (**198d**).



To (trimethylsilyl)acetylene (1.39 g, 14.2 mmol) in diethyl ether (20 mL) at -78°C was added *n*-BuLi (5.7 mL, 2.5 M in hexanes, 14.3 mmol). After stirring for 0.5 h, 3-methoxybenzaldehyde (1.75 g, 12.9 mmol) was added and the general procedure was followed to give **198d** (2.29 g, 76%) as a light yellow oil: $R_f = 0.41$ (hexanes/ Et_2O 7:3); IR (CHCl_3 cast) 3405, 2959, 2173, 1601, 1251, 1040 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.29 (t, $J = 8.0$ Hz, 1H), 7.12 (m, 2H), 6.86 (m, 1H), 5.41 (s, 1H), 3.81 (s,

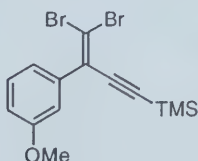
3H), 3.05 (s, 1H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 159.5, 141.9, 129.5, 119.0, 114.1, 111.9, 105.1, 91.2, 64.6, 55.1, -0.3 ; EI HRMS m/z calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2\text{Si}$ (M^+) 234.1076, found 234.1072.

1-(3-Methoxyphenyl)-3-trimethylsilylpropynone (199d).



To alcohol **198d** (0.405 g, 1.73 mmol) in CH_2Cl_2 were sequentially added Celite (0.5 g), molecular sieves ($4\text{\AA}$, 0.5 g), and PCC (0.45 g, 2.09 mmol) as per the general procedure to give the ketone **199d** (0.305 g, 76%) as a bright yellow oil: R_f = 0.75 (hexanes/ Et_2O 7:3); IR (CHCl_3 cast) 3005, 2961, 2153, 1647, 1269, 1028 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73 (m, 1H), 7.58 (m, 1H), 7.34 (m, 1H), 7.10 (m, 1H), 3.80 (s, 3H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 177.2, 159.7, 137.8, 129.5, 122.7, 121.0, 112.8, 100.8, 100.2, 55.3, -0.8 . MS (EI, 70 eV) m/z 232.1 (M^+ , 82), 217.1 ($[\text{M} - \text{CH}_3]^+$, 100). EI HRMS m/z calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2\text{Si}$ (M^+) 232.0920, found 232.0918.

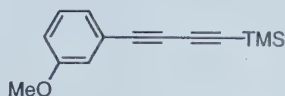
[4,4-Dibromo-3-(3-methoxyphenyl)-buten-1-ynyl]trimethylsilane (200d).



To **198d** (0.508 g, 2.17 mmol) in CH_2Cl_2 were sequentially added Celite (0.6 g), molecular sieves ($4\text{\AA}$, 0.6 g), and PCC (0.585 g, 2.69 mmol) as per the general procedure to give ketone **199d** that, following workup, was subjected to dibromoolefination using CBr_4 (0.876 g, 2.64 mmol) and PPh_3 (1.36 g, 5.20 mmol) in CH_2Cl_2 (80 mL) to give **200d** (0.407 g, 48%) as an oil: R_f = 0.3 (hexanes); IR (CHCl_3 cast) 2958, 2834, 2145, 1597, 1250 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.31 (t, J = 8.0 Hz, 1H), 7.05 (m, 1H), 7.03 (m, 1H), 6.91 (m, 1H), 3.84 (s, 3H), 0.24 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 159.4, 139.0, 130.8, 129.4, 120.9, 114.3, 114.1, 104.2,

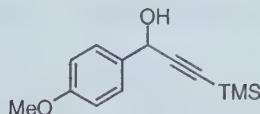
103.3, 100.5, 55.3, -0.3; EI HRMS m/z calcd for $C_{14}H_{16}OSi^{79}Br^{81}Br$ (M^+) 387.9317, found 387.9314.

[4-(3-Methoxyphenyl)-1,3-butadiynyl]trimethylsilane (201d).



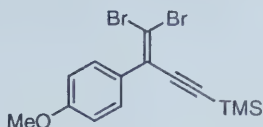
Dibromoolefin **200d** (152 mg, 0.392 mmol) was reacted with *n*-BuLi (0.16 mL, 2.5 M in hexanes, 0.40 mmol) as per the general procedure to give diyne **201d** (67.3 mg, 75%) as a yellow oil: R_f = 0.8 (hexanes/ CH_2Cl_2 1:1); IR ($CHCl_3$ cast) 3004, 2959, 2207, 2102, 1596, 1574, 1251 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.22 (t, J = 7.5 Hz, 1H), 7.09 (ddd, J = 1.0, 1.3, 7.5 Hz, 1H), 7.02 (dd, J = 1.3, 2.5 Hz, 1H), 6.93 (ddd, J = 7.5, 2.5, 1.0 Hz, 1H), 3.80 (s, 3H), 0.26 (s, 9H); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 159.3, 129.6, 125.3, 122.4, 117.3, 116.2, 90.7, 87.9, 76.7, 74.0, 55.3, -0.4; EI HRMS m/z calcd for $C_{14}H_{16}OSi$ (M^+) 228.0971, found 228.0966.

1-(4-Methoxyphenyl)-3-trimethylsilylprop-2-yn-1-ol (198e).*



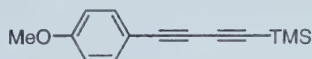
To (trimethylsilyl)acetylene (1.30 g, 14.0 mmol) in diethyl ether (30 mL) at -78 °C was added *n*-BuLi (5.7 mL, 2.4 M in hexanes, 13.7 mmol). After stirring for 0.5 h, 4-methoxybenzaldehyde (1.52 g, 11.2 mmol) was added and the general procedure was followed to give **198e** (2.54 g, 97%) as a light yellow oil: R_f = 0.79 (hexanes/ Et_2O 7:3); IR ($CHCl_3$ cast) 3407, 2959, 2173, 1587, 1250, 1037 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 5.38 (d, J = 5.5 Hz, 1H), 3.78 (s, 3H), 2.41 (bs, 1H), 0.19 (s, 9H); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 159.6, 132.7, 128.1, 113.9, 105.4, 91.1, 64.4, 55.2, -0.2; EI HRMS m/z calcd for $C_{13}H_{18}O_2Si$ (M^+) 234.1076, found 234.1070. *Previously reported by: Brown, R. F. C.; Jackson, W. R.; McCarthy, T. D. *Tetrahedron* **1994**, 50, 5469-5488.

[4,4-Dibromo-3-(4-methoxyphenyl)buten-1-ynyl]trimethylsilane (200e).



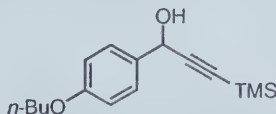
To **198e** (1.90 g, 8.10 mmol) in CH_2Cl_2 were sequentially added Celite (2.5 g), molecular sieves ($4\text{\AA}$, 2.5 g), and PCC (2.28 g, 10.6 mmol) as per the general procedure. The resulting ketone **199e** was subjected directly to dibromoolefination conditions, using CBr_4 (3.50 g, 10.6 mmol) and PPh_3 (5.57 g, 21.3 mmol) as per the general procedure to give **200e** (1.47 g, 47%) as a light yellow oil: $R_f = 0.6$ (hexanes/ CH_2Cl_2 2:1); IR (CH_2Cl_2 cast) 3001, 2959, 2183, 2136, 1607, 1249, 1079 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.45 (d, $J = 9.0$ Hz, 2H), 6.92 (d, $J = 9.0$ Hz, 2H), 3.86 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 159.6, 130.5, 130.0, 129.9, 113.6, 103.7, 103.6, 99.4, 55.2, 0.1; EI HRMS m/z calcd for $\text{C}_{14}\text{H}_{16}\text{OSi}^{79}\text{Br}^{81}\text{Br}$ (M^+) 387.9317, found 387.9318.

[4-(4-Methoxyphenyl)-1,3-butadiynyl]trimethylsilane (201e).*



Dibromoolefin **200e** (139 mg, 0.358 mmol) was reacted with $n\text{-BuLi}$ (0.15 mL, 2.5 M in hexanes, 0.38 mmol) as per the general procedure to give diyne **201e** (67.2 mg, 82%) as a yellow oil. *Spectral data were consistent with those reported by: Wan, W. B.; Haley, M. M. *J. Org. Chem.* **2001**, 66, 3893–3901.

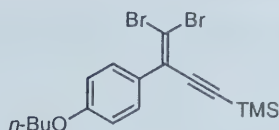
1-(4-*n*-Butoxyphenyl)-3-trimethylsilylprop-2-yn-1-ol (198f).



To (trimethylsilyl)acetylene (0.61 g, 6.2 mmol) in diethyl ether (20 mL) at -78°C was added $n\text{-BuLi}$ (2.36 mL, 2.5 M in hexanes, 5.90 mmol). After stirring for 0.5 h, 4-butoxybenzaldehyde (0.97 g, 5.47 mmol) was added and the general procedure was followed to give **198f** (1.04 g, 69%) as a yellow oil: $R_f = 0.13$ (hexanes/ Et_2O 7:3); IR

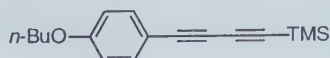
(CH₂Cl₂ cast) 3404, 2959, 2873, 2173, 1611, 1585, 1511, 1475, 1250 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.42 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.40 (s, 1H), 3.94 (t, *J* = 6.5 Hz, 2H), 2.10 (bs, 1H), 1.74 (quint, *J* = 6.7 Hz, 2H), 1.46 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.18 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 159.4, 132.5, 128.2, 114.6, 105.3, 91.3, 67.8, 64.7, 31.3, 19.3, 13.9, -0.1; EI HRMS *m/z* calcd for C₁₆H₂₄O₂Si (M⁺) 276.1546, found 276.1538.

[4,4-Dibromo-3-(4-*n*-butoxyphenyl)buten-1-ynyl]trimethylsilane (200f).



To **198f** (0.608 g, 2.17 mmol) in CH₂Cl₂ were sequentially added Celite (0.6 g), molecular sieves (4Å, 0.6 g), and PCC (0.58 g, 2.64 mmol) as per the general procedure. The resulting ketone **199f** was subjected directly to dibromoolefination conditions, using CBr₄ (0.87 g, 2.60 mmol) and PPh₃ (1.48 g, 5.59 mmol). The reaction mixture was stirred overnight. Since TLC monitoring of the reaction showed that the reaction had not reached completion, more of the brominating mixture (0.4 equiv of CBr₄ and 0.8 equiv PPh₃) was added. Work-up as per the general procedure and purification by column chromatography (hexanes) yielded **200f** (0.363 g, 38%) as a yellow oil: *R_f* = 0.9 (hexanes/CH₂Cl₂ 1:1); IR (CH₂Cl₂ cast) 2958, 2172, 2134, 1606, 1506, 1469, 1249 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.38 (d, *J* = 8.9 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 3.97 (t, *J* = 6.5 Hz, 2H), 1.77 (quint, *J* = 6.6 Hz, 2H), 1.49 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.21 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 159.2, 130.6, 129.9, 129.7, 114.1, 103.7, 103.6, 99.2, 67.8, 31.4, 19.4, 14.0, -0.2; MS (EI, 70 eV) *m/z* 430.0 (M⁺, 100).

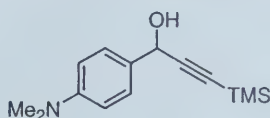
[4-(4-*n*-Butoxyphenyl)-1,3-butadiynyl]trimethylsilane (201f).



Dibromoolefin **200f** (200 mg, 0.464 mmol) was reacted with *n*-BuLi (0.19 mL, 2.5 M in hexanes, 0.48 mmol) as per the general procedure to give diyne **201f** (99 mg, 79%)

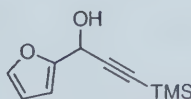
as a yellow solid: mp 68-69 °C; R_f = 0.9 (hexanes/Et₂O 4:1); IR (CH₂Cl₂ cast) 2956, 2940, 2871, 2203, 2101, 1602, 1508, 1257 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.42 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 3.96 (t, J = 7.2 Hz, 2H), 1.76 (m, 2H), 1.48 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H), 0.22 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 160.1, 134.3, 114.7, 113.0, 89.8, 88.2, 77.2, 73.0, 67.9, 31.2, 19.2, 13.8, -0.3; MS (EI, 70 eV) m/z 270.1 (M⁺, 78), 199.1 ([M - C₄H₈ - CH₃]⁺, 100); EI HRMS m/z calcd for C₁₇H₂₂OSi (M⁺) 270.1440, found 270.1436.

1-(4-Dimethylaminophenyl)-3-trimethylsilylprop-2-yn-1-ol (198g).



To (trimethylsilyl)acetylene (1.39 g, 14.2 mmol) in diethyl ether (20 mL) at -78 °C was added *n*-BuLi (5.4 mL, 2.5 M in hexanes, 13.6 mmol). After stirring for 0.5 h, dimethylaminobenzaldehyde (1.93 g, 12.9 mmol) was added and the general procedure was followed to give **198g** (2.90 g, 91%) as a yellow-green crystalline solid: mp 94-96 °C; R_f = 0.31 (hexanes/Et₂O 7:3); IR (CHCl₃ cast) 3376, 2958, 2896, 2169, 1614, 1522, 1249 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.43 (d, J = 9.0 Hz, 2H), 6.75 (d, J = 9.0 Hz, 2H), 5.39 (d, J = 5.0 Hz, 1H), 2.98 (s, 6H), 3.78 (d, J = 5.0 Hz, 1H), 0.23 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 150.6, 128.6, 127.9, 112.5, 105.8, 90.5, 64.7, 40.6, -0.3; EI HRMS m/z calcd for C₁₄H₂₁ONSi (M⁺) 247.1392, found 247.1387.

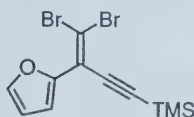
1-(2-Furyl)-3-trimethylsilylprop-2-yn-1-ol (198h).



To (trimethylsilyl)acetylene (2.10 g, 21.3 mmol) in diethyl ether (30 mL) at -78 °C was added *n*-BuLi (8.5 mL, 2.4 M in hexanes, 20.4 mmol). After stirring for 0.5 h, 2-furaldehyde (1.83 g, 19.0 mmol) was added and the general procedure was followed to give **198h** (3.15 g, 85%) as a light yellow oil: R_f = 0.60 (hexanes/Et₂O 7:3); IR (CHCl₃

cast) 3377, 2960, 2178, 1251 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.36 (m, 1H), 6.42 (m, 1H), 6.29 (m, 1H), 5.38 (d, $J = 6.1$ Hz, 1H), 3.30 (bs, 1H), 0.18 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 152.9, 142.8, 110.2, 107.7, 102.6, 90.4, 58.2, -0.4 ; MS (EI, 70 eV) m/z 194.1 (M^+ , 64), 99.0 ($[\text{M} - \text{C}_6\text{H}_7\text{O}]^+$, 100); HRMS m/z calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2\text{Si}$ (M^+) 194.0763, found 194.0757. Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2\text{Si}$: C, 61.81; H, 7.26. Found C, 61.86; H, 7.28.

[4,4-Dibromo-3-(2-furyl)buten-1-ynyl]trimethylsilane (**200h**).



To **198h** (1.90 g, 9.80 mmol) in CH_2Cl_2 were sequentially added Celite (3.0 g), molecular sieves ($4\text{\AA}$, 3.0 g), and PCC (2.68 g, 12.5 mmol) as per the general procedure. The resulting ketone **199h*** was subjected directly to dibromoolefination conditions, using CBr_4 (4.05 g, 12.5 mmol) and PPh_3 (6.42 g, 24.5 mmol) as per the general procedure to give **200h** (1.15 g, 34%) as an oil which decomposes readily even when refrigerated: $R_f = 0.85$ (hexanes/ Et_2O 4:1); IR (CHCl_3 cast) 2959, 2148, 1250 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.50 (dd, $J = 1.9, 0.7$ Hz, 1H), 6.90 (dd, $J = 4.3, 0.7$ Hz, 1H), 6.46 (dd, $J = 4.3, 1.9$ Hz, 1H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 149.0, 142.9, 120.8, 112.9, 111.3, 103.2, 101.3, 97.3, -0.3 ; EI HRMS m/z calcd for $\text{C}_{11}\text{H}_{12}\text{OSi}^{79}\text{Br}^{81}\text{Br}$ (M^+) 347.9004, found 347.9006. *Previously reported by: Walton, D. R. M.; Waugh, F. J. *Organomet. Chem.* **1972**, 37, 45-56.

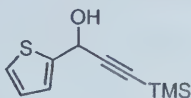
[4-(2-Furyl)-1,3-butadiynyl]trimethylsilane (**201h**).



Dibromoolefin **200h** (126 mg, 0.362 mmol) was reacted with *n*-BuLi (0.15 mL, 2.5 M in hexanes, 0.38 mmol) as per the general procedure to give diyne **201h** (37.1 mg, 54%) as a light yellow oil that slowly decomposes, even if kept refrigerated; $R_f = 0.9$ (hexanes/ CH_2Cl_2 1:1); IR (CH_2Cl_2 cast) 2960, 2201, 2104, 1251 cm^{-1} ; ^1H NMR (300 MHz, CD_2Cl_2) δ 7.43 (dd, $J = 2.0, 0.1$ Hz, 1H), 6.77 (dd, $J = 3.3, 0.7$ Hz, 1H), 6.43

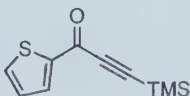
(dd, $J = 3.3, 0.7$ Hz, 1H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CD_2Cl_2) δ 145.4, 136.5, 119.1, 111.6, 94.6, 87.2, 79.2, 66.4, -0.4 ; MS (EI, 70 eV) m/z 188.1 (M^+ , 44), 173.0 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{11}\text{H}_{12}\text{OSi}$ (M^+) 188.0658, found 188.0662.

1-(2-Thienyl)-3-trimethylsilylprop-2-yn-1-ol (**198i**).



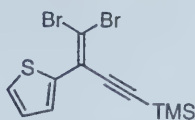
To (trimethylsilyl)acetylene (2.10 g, 21.3 mmol) in diethyl ether (30 mL) at -78°C was added *n*-BuLi (8.5 mL, 2.4 M in hexanes, 20.4 mmol). After stirring for 0.5 h, 2-thiophene carboxaldehyde (2.17 g, 19.0 mmol) was added and the general procedure was followed to give **198i** (3.88 g, 97%) as a light yellow oil: $R_f = 0.56$ (hexanes/ Et_2O 7:3); IR (CHCl_3 cast) 3377, 3106, 2960, 2175, 1251 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.30 (dd, $J = 5.0, 1.1$ Hz, 1H), 7.16 (m, 1H), 6.98 (dd, $J = 5.0, 3.5$ Hz, 1H), 5.63 (d, $J = 6.0$ Hz, 1H), 3.00 (s, 1H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 144.3, 126.7, 126.0, 125.6, 104.3, 91.0, 60.4, -0.3 ; EI HRMS m/z calcd for $\text{C}_{10}\text{H}_{14}\text{OSSi}$ (M^+) 210.0535, found 210.0533. Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{OSSi}$: C, 57.09; H, 6.71. Found C, 57.32; H, 6.58.

1-(2-Thienyl)-3-trimethylsilylpropynone (**199i**).



The alcohol **198i** (1.47 g, 6.96 mmol) was oxidized using PCC (2.30 g, 10.5 mmol) in the presence of Celite (2.3 g) and molecular sieves ($4\text{\AA}$, 2.3 g) as per the general procedure to give the ketone **199i** (1.26 g, 87%) as a yellow oil: $R_f = 0.65$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 3105, 2961, 2900, 2153, 1625, 1265 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.91 (dd, $J = 4.0, 1.0$ Hz, 1H), 7.69 (dd, $J = 5.0, 1.0$ Hz, 1H), 7.14 (dd, $J = 5.0, 4.0$ Hz, 1H), 0.30 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 169.5, 144.7, 135.6, 135.4, 128.3, 100.5, 99.2, -0.7 ; MS (EI, 70 eV) m/z 208.0 (M^+ , 69), 193.0 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{10}\text{H}_{12}\text{OSiS}$ (M^+) 208.0378, found 208.0378.

[4,4-Dibromo-3-(2-thienyl)buten-1-ynyl]trimethylsilane (200i).



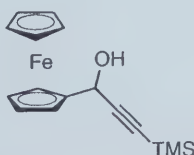
Ketone **199i** (0.424 g, 2.04 mmol) was reacted with CBr_4 (0.852 g, 2.54 mmol) and PPh_3 (1.35 g, 5.09 mmol) as per the general procedure to give **200i** (0.628 g, 85%) as a yellow oil: $R_f = 0.77$ (hexanes/ Et_2O 4:1); IR (CHCl_3 cast) 2959, 2898, 2153, 1249 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.67 (dd, $J = 4.0, 1.1$ Hz, 1H), 7.40 (dd, $J = 5.0, 1.1$ Hz, 1H), 7.06 (dd, $J = 5.0, 4.0$ Hz, 1H), 0.38 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.4, 130.6, 127.6, 126.6, 124.4, 103.5, 102.9, 97.5, -0.3 ; EI HRMS m/z calcd for $\text{C}_{11}\text{H}_{12}\text{SiS}^{79}\text{Br}^{81}\text{Br}$ (M^+) 363.8775, found 363.8779.

[4-(2-Thienyl)-1,3-butadiynyl]trimethylsilane (201i).



Dibromoolefin **200i** (582 mg, 1.60 mmol) was reacted with $n\text{-BuLi}$ (0.77 mL, 2.5 M in hexanes, 1.93 mmol) as per the general procedure to give diyne **201i** (298 mg, 91%) as a light brown oil that slowly decomposes, even if kept refrigerated; $R_f = 0.9$ (CH_2Cl_2 /hexanes 1:1); IR (CHCl_3 cast) 3107, 2960, 2194, 2101, 1251 cm^{-1} ; ^1H NMR (300 MHz, CD_2Cl_2) δ 7.31 (m, 2H), 7.10 (m, 1H), 0.17 (s, 9H); ^{13}C NMR (75 MHz, APT, CD_2Cl_2) δ 134.7, 128.9, 127.2, 121.7, 93.0, 87.6, 78.3, 69.8, -0.4 ; MS (EI, 70 eV) m/z 204.0 (M^+ , 37), 189.0 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{11}\text{H}_{12}\text{SSi}$ (M^+) 204.0429, found 204.0424.

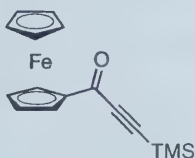
1-Ferrocenyl-3-trimethylsilylprop-2-yn-1-ol (198k).



To (trimethylsilyl)acetylene (1.30 g, 14.0 mmol) in diethyl ether (30 mL) at -78°C was added $n\text{-BuLi}$ (5.7 mL, 2.4 M in hexanes, 13.7 mmol). After stirring for 0.5 h,

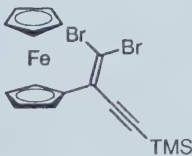
ferrocene carboxaldehyde (2.40 g, 11.2 mmol) was added and the general procedure was followed to give **198k** (3.31 g, 95%) as an orange solid: mp 51-52 °C; R_f = 0.41 (hexanes/Et₂O 7:3); IR (CHCl₃ cast) 3388, 3097, 2958, 2174, 1250 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.15 (d, J = 7.5 Hz, 1H), 4.40 (m, 1H), 4.33 (m, 1H), 4.20 (m, 7H), 2.20 (d, J = 7.5 Hz, 1H), 0.28 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 105.4, 89.2, 88.9, 68.9, 68.5, 66.5, 61.4, 0.2 (two coincident signals not observed); EI HRMS m/z calcd for C₁₆H₂₀OSiFe (M⁺) 312.0633, found 312.0633.

1-Ferrocenyl-3-trimethylsilylpropynone (199k).



To **198k** (0.31 g, 0.99 mmol) in CH₂Cl₂ (70 mL) was added barium manganate (0.76 g, 3.0 mmol). After stirring for 1h, the reaction mixture was filtered through Celite and the solvent was evaporated to give **199k** (0.29 g, 94%) as a red solid: mp 68-69 °C; IR (CHCl₃ cast) 2958, 2029, 1626, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.90 (t, J = 2.0 Hz, 2H), 4.59 (t, J = 2.0 Hz, 2H), 4.24 (s, 5H), 0.30 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 180.9, 102.2, 96.3, 80.3, 73.6, 73.4, 70.7, -0.5; EI HRMS m/z calcd for C₁₆H₁₈OSiFe (M⁺) 310.0476, found 310.0475.

[4,4-Dibromo-3-ferrocenyl-buten-1-ynyl]trimethylsilane (200k).



To **198k** (0.680 g, 2.20 mmol) in CH₂Cl₂ (50 mL) were sequentially added Celite (0.6 g), molecular sieves (4Å, 0.6 g), and PCC (0.58 g, 2.70 mmol). The reaction mixture was stirred and monitored by TLC. Upon completion of the reaction, the reaction mixture was passed through a plug of silica (CH₂Cl₂) and was used directly in the next step. The solution was diluted with 70 mL of benzene and CBr₄ (0.883 g, 2.64 mmol) and PPh₃ (1.50 g, 5.66 mmol) were added. The reaction mixture was refluxed for 2

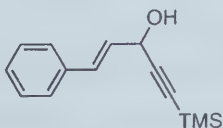
days and the general work-up procedure was then carried out to give **200k** (0.265 g, 26%) as an orange oil: $R_f = 0.84$ (hexanes/Et₂O 4:1); IR (CH₂Cl₂ cast) 3096, 2958, 2152, 1249 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 4.71 (t, $J = 2.0$ Hz, 2H), 4.08 (s, 5H), 4.02 (t, $J = 2.0$ Hz, 2H), 0.22 (s, 9H); ¹³C NMR (100 MHz, APT, C₆D₆) δ 129.6, 104.4, 101.9, 94.4, 82.4, 70.5, 70.4, 69.2, -0.2; EI HRMS m/z calcd for C₁₇H₁₈OSi⁷⁹Br⁸¹BrFe (M⁺) 465.8874, found 465.8874.

(4-Ferrocenyl-1,3-butadiynyl)trimethylsilane (**201k**).



To dibromoolefin **200k** (153 mg, 0.373 mmol) in dry hexanes (10 mL) at -78 °C was added dropwise over ten minutes, one equivalent of *n*-BuLi (0.16 mL, 2.5 M in hexanes, 0.40 mmol). The mixture was warmed to -20 °C, cooled to -78 °C and an additional quarter equivalent of *n*-BuLi (0.04 mL, 2.5 M in hexanes) was added. Work-up as per the general procedure and purification via column chromatography (hexanes/CH₂Cl₂ 2:1) gave diyne **201k** (32 mg, 28%) as an orange oil: $R_f = 0.7$ (hexanes/CH₂Cl₂ 1:1); IR (CH₂Cl₂ cast) 2925, 2205, 2102, 1249 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.49 (t, $J = 1.8$ Hz, 2H), 4.25 (s, 5H), 4.24 (t, $J = 1.8$ Hz, 2H), 0.23 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 88.7, 87.6, 77.3, 72.3, 70.5, 70.2, 69.4, 62.5, -0.3; EI HRMS m/z calcd for C₁₇H₁₈SiFe (M⁺) 306.0527, found 306.0530.

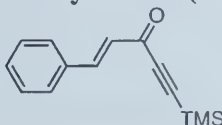
1-Phenyl-5-trimethylsilylpent-1-en-4-yn-3-ol (**198l**).



To (trimethylsilyl)acetylene (1.39 g, 14.2 mmol) in diethyl ether (20 mL) at -78 °C was added *n*-BuLi (5.7 mL, 2.5 M in hexanes, 14.3 mmol). After stirring for 0.5 h, cinnamaldehyde (1.72 g, 13.0 mmol) was added and the general procedure was followed to give **198l** (2.40 g, 81%) as a light yellow oil: $R_f = 0.36$ (hexanes/Et₂O 7:3); IR (CHCl₃ cast) 3359, 3027, 2969, 2172, 1627, 1251 cm⁻¹; ¹H NMR (400 MHz,

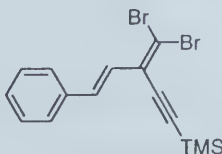
CDCl₃) δ 7.40 (m, 2H), 7.30 (m, 3H), 6.77 (d, J = 15.8 Hz, 1H), 6.29 (dd, J = 15.8, 6.0 Hz, 1H), 5.05 (m, 1H), 2.39 (bs, 1H), 0.23 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 136.1, 132.0, 128.6, 128.1, 128.0, 126.8, 104.4, 91.3, 63.3, -0.1; MS (EI, 70 eV) m/z 230.1 (M⁺, 49), 73.0 ([Me₃Si]⁺, 100); EI HRMS m/z calcd for C₁₄H₁₈OSi (M⁺) 230.1127, found 230.1120. Anal. Calcd for C₁₄H₁₈OSi: C, 72.99; H, 7.88. Found C, 72.92; H, 8.21.

1-Phenyl-5-trimethylsilylpent-1-en-4-yn-3-one (**199l**).*



The alcohol **198l** (0.436 g, 1.89 mmol) was oxidized using barium manganate (1.46 g, 5.68 mmol) as per the general procedure to give the ketone **199l** (0.416 g, 96%) as a yellow oil: R_f = 0.74 (CH₂Cl₂); IR (CHCl₃ cast) 3061, 3027, 2961, 2901, 2157, 1653, 1630, 1599, 1576, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, J = 16.1 Hz, 1H), 7.54 (m, 2H), 7.40 (m, 3H), 6.75 (d, J = 16.1 Hz, 1H), 0.29 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 177.9, 148.8, 134.0, 131.2, 129.0, 128.6, 128.2, 100.6, 98.6, -0.7; EI HRMS m/z calcd for C₁₄H₁₆OSi (M⁺) 228.0971, found 228.0967. *Previously reported by: Walton, D. R. M.; Waugh, F. *J. Organomet. Chem.* **1972**, 37, 45-56.

(3-Dibromomethylene-5-phenylpent-4-en-1-ynyl)trimethylsilane (**200l**).



The alcohol **198l** (0.499 g, 2.16 mmol) was oxidized using barium manganate (1.60 g, 5.62 mmol) and after passing through a plug of silica (CH₂Cl₂), the resulting ketone **199l** was subjected to general dibromoolefination conditions without additional purification using CBr₄ (1.45 g, 4.36 mmol) and PPh₃ (2.29 g, 8.73 mmol) to give **200l** (0.641 g, 77%) as a yellow oil: R_f = 0.97 (CH₂Cl₂); IR (CHCl₃ cast) 3058, 3025, 2959, 2146, 1250 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.50 (m, 2H), 7.35 (m, 3H), 7.20 (d, J = 15.6 Hz, 1H), 7.06 (d, J = 15.6 Hz, 1H), 0.32 (s, 9H); ¹³C NMR (100 MHz, APT,

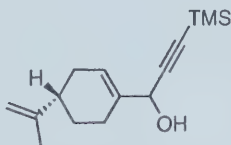
CDCl₃) δ 136.4, 136.3, 128.82, 128.76, 128.7, 127.2, 124.7, 104.9, 100.6, 99.8, -0.2; MS (EI, 70 eV) m/z 381.9/383.9/385.9 (M^+ , 29/54/29); HRMS m/z calcd for C₁₅H₁₆Si⁷⁹Br₂/C₁₅H₁₆S⁷⁹Br⁸¹Br/C₁₅H₁₆S⁸¹Br₂ (M^+) 381.9388/383.9368/385.9347, found 381.9416/383.9386/385.9347. Anal. Calcd for C₁₅H₁₆SiBr₂: C, 46.89; H, 4.20. Found C, 46.73; H, 4.23.

(6-Phenyl-hex-5-ene-1,3-diynyl)trimethylsilane (201I).



Dibromoolefin **200I** (610 mg, 1.59 mmol) was reacted with *n*-BuLi (0.76 mL, 2.5 M in hexanes, 1.9 mmol) as per the general procedure to give diyne **201I** (338 mg, 95%) as a yellow oil: R_f = 0.4 (hexanes); IR (CHCl₃ cast) 3030, 2959, 2925, 2191, 2092, 1605, 1492, 1448 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.34 (m, 5H), 7.08 (d, J = 16.2 Hz, 1H), 6.16 (d, J = 16.2 Hz, 1H), 0.22 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 145.1, 135.6, 129.3, 128.8, 126.4, 106.3, 91.3, 88.0, 76.5, 76.3, -0.4; MS (EI, 70 eV) m/z 224.1 (M^+ , 50), 209.1 ([M - CH₃]⁺, 100); EI HRMS m/z calcd for C₁₅H₁₆Si (M^+) 224.1021, found 224.1020.

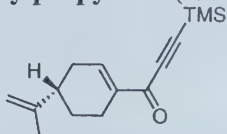
1-[(*S*)-(-)-perillyl]-3-trimethylsilylprop-2-yn-1-ol (198m).



To (trimethylsilyl)acetylene (1.11 g, 11.0 mmol) in diethyl ether (40 mL) at -78 °C was added *n*-BuLi (4.0 mL, 2.5 M in hexanes, 10.1 mmol). After stirring for 30 minutes, (*S*)-(-)-perillaldehyde (1.37 g, 9.14 mmol) dissolved in 5 mL of ether was added and stirring was continued for 2 h at -78 °C. The reaction was quenched with sat. aq. NH₄Cl at -78 °C, extracted with ether, and dried (Na₂SO₄). Column chromatography (CH₂Cl₂/hexanes, 1:2) gave **198m** (1.42 g, 63%) as a colorless oil which upon refrigeration turned into a clear waxy solid: mp 30-31 °C; R_f = 0.44 (CH₂Cl₂); IR (CH₂Cl₂ cast) 3332, 3082, 2962, 2920, 2839, 2170, 1644 cm⁻¹; [α]_D²² -50.5° (c = 0.0020, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 5.91 (s, 1H), 4.72 (m,

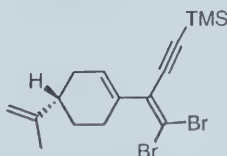
3H), 2.15 (m, 4H), 1.98 (m, 1H), 1.87 (m, 2H), 1.73 (s, 3H), 1.48 (m, 1H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 149.6, 136.4, 124.4, 108.8, 104.8, 90.9, 66.9, 40.9, 30.6, 27.5, 24.7, 20.8, -0.1; MS (EI, 70 eV) m/z 248.2 (M^+ , 23), 73.0 (Me_3Si^+ , 100); HRMS m/z calcd for $\text{C}_{15}\text{H}_{24}\text{OSi}$ (M^+) 248.1596, found 248.1599. Anal. Calcd for $\text{C}_{15}\text{H}_{24}\text{OSi}$: C, 72.52; H, 9.74. Found C, 72.04; H, 10.34.

1-[(S)-(-)-perillyl]-3-trimethylsilylpropynone (**199m**).



To **198m** (0.464 g, 1.87 mmol) in CH_2Cl_2 (20 mL) was added barium manganate (1.60 g, 5.60 mmol). After stirring for 1h, the reaction mixture was filtered through Celite. The solvent was evaporated and the crude product was purified by column chromatography (hexanes/ CH_2Cl_2 2:1) to give **199m** (0.390 g, 85%) as a colorless oil: R_f = 0.65 (CH_2Cl_2); IR (CHCl_3 cast) 3082, 2962, 2936, 2151, 1631, 1452, 1251 cm^{-1} ; $[\alpha]_D^{22}$ -85.7° (c = 0.0074, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 7.36 (m, 1H), 4.76 (s, 1H), 4.72 (s, 1H), 2.49 (m, 2H), 2.19 (m, 3H), 1.89 (m, 1H), 1.74 (s, 3H), 1.42 (m, 1H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 178.6, 148.1, 146.8, 139.7, 109.1, 99.9, 97.4, 39.9, 31.5, 26.3, 22.4, 20.4, -1.0; MS (EI, 70 eV) m/z 246.1 (M^+ , 46); HRMS m/z calcd for $\text{C}_{15}\text{H}_{22}\text{OSi}$ (M^+) 246.1440, found 246.1434; Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{OSi}$: C, 73.11; H, 9.00. Found C, 72.96; H, 8.92.

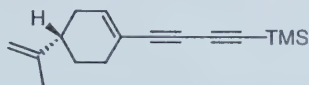
[4-Dibromomethylene-3-[(S)-(-)-perillyl]-but-3-en-1-ynyl]trimethylsilane (**200m**).



CBr_4 (0.499 g, 1.49 mmol) and PPh_3 (1.184 g, 4.47 mmol) were added to CH_2Cl_2 (20 mL) and the mixture stirred for 5 min at rt. Ketone **199m** (0.122 g, 0.50 mmol) in CH_2Cl_2 (5 mL) was added in one portion. The reaction mixture was stirred for 4 h, concentrated to ca. 15 mL, hexanes (15 mL) added, and the inhomogeneous mixture was filtered through Celite. Evaporation gave a yellow oil which was purified by

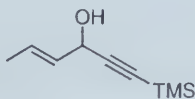
passing through a plug of silica (hexanes) to give **200m** (0.054 g, 27%) as a bright yellow oil: $R_f = 0.38$ (hexanes); IR (CH_2Cl_2 cast) 2958, 2920, 2850, 2145, 1249 cm^{-1} ; $[\alpha]_D -23.3^\circ$ ($c = 0.0096$, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 5.79 (s, 1H), 4.73 (s, 2H), 2.18 (m, 4H), 2.01 (m, 1H), 1.84 (m, 1H), 1.73 (s, 3H), 1.52 (m, 1H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 149.2, 135.3, 132.8, 129.0, 108.9, 103.2, 102.2, 98.7, 40.2, 30.7, 27.4, 27.2, 20.7, -0.3 ; MS (EI, 70 eV) m/z 400.0/402.0/404.0 (M^+ , 29/43/22); HRMS m/z calcd for $\text{C}_{16}\text{H}_{22}\text{Si}^{79}\text{Br}_2/\text{C}_{16}\text{H}_{22}\text{Si}^{79}\text{Br}^{81}\text{Br}/\text{C}_{16}\text{H}_{22}\text{Si}^{81}\text{Br}_2$ (M^+) 399.9858/401.9837/403.9817, found 399.9793/401.9819/403.9814.

[4-(*S*)-(-)-Perillyl-1,3-butadienyl]trimethylsilane (**201m**).



Dibromoolefin **200m** (131 mg, 0.324 mmol) was reacted with *n*-BuLi (0.16 mL, 2.5 M in hexanes, 0.40 mmol) as per the general procedure to give diyne **201m** (37 mg, 46%) as a pale yellow oil which solidified into a yellow solid upon refrigeration: mp 52–54°C; $R_f = 0.3$ (hexanes); IR (CH_2Cl_2 cast) 3082, 2960, 2198, 2098, 1676, 1645 cm^{-1} ; $[\alpha]_D^{22} -17.2^\circ$ ($c = 0.0029$, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 6.29 (m, 1H), 4.73 (m, 1H), 4.69 (m, 1H), 2.20 (m, 3H), 2.10 (m, 1H), 2.03 (m, 1H), 1.80 (m, 1H), 1.71 (s, 3H), 1.45 (m, 1H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 148.8, 138.7, 119.1, 109.2, 89.4, 88.1, 78.5, 72.0, 39.8, 31.3, 28.9, 27.0, 20.6, -0.4 ; MS (EI, 70 eV) m/z 242.1 (M^+ , 51); EI HRMS m/z calcd for $\text{C}_{16}\text{H}_{22}\text{Si}$ (M^+) 242.1491, found 242.1491.

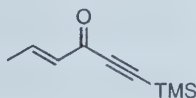
1-Trimethylsilyl-hex-4-en-1-yn-3-ol (**198n**).



To (trimethylsilyl)acetylene (1.72 g, 17.1 mmol) in diethyl ether (60 mL) at -78°C was added *n*-BuLi (6.3 mL, 2.5 M in hexanes, 15.7 mmol). After stirring for 30 minutes, crotonaldehyde (1.00 g, 14.3 mmol, 1.19 mL) was added and stirring was continued for 2 h at -78°C . The reaction was quenched with sat. aq. NH_4Cl at -78°C , extracted with ether, and dried (Na_2SO_4). Column chromatography (hexanes/ CH_2Cl_2

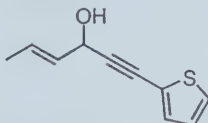
2:1) gave **198n** (0.930 g, 39%) as a pale yellow oil: $R_f = 0.4$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 3329, 3031, 2961, 2918, 2899, 2173, 1449, 1251 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.86 (m, 1H), 5.61 (m, 1H), 4.79 (t, $J = 6.1$ Hz, 1H), 1.87 (d, $J = 6.0$ Hz, 1H), 1.71 (dd, $J = 6.5, 1.1$ Hz, 3H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 129.9, 129.0, 104.8, 90.5, 63.3, 17.5, -0.2; MS (EI, 70 eV) m/z 168.1 (M^+ , 54); HRMS m/z calcd for $\text{C}_9\text{H}_{16}\text{OSi}$ (M^+) 168.0971, found 168.0971.

1-Trimethylsilyl-hex-4-en-1-yn-3-one (**199n**).



To **198n** (0.010 g, 0.59 mmol) in CH_2Cl_2 was added 3 equivalents of barium manganate (0.505 g, 1.77 mmol). After stirring for 1h, the reaction mixture was filtered through Celite. The solvent was evaporated to give **199n** (0.087 g, 89%) as a yellow oil: IR (CHCl_3 cast) 3037, 2963, 2902, 2156, 1663, 1641, 1628, 1442, 1253 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.16 (dq, $J = 15.4, 6.8$ Hz, 1H), 6.12 (dq, $J = 15.4, 1.6$ Hz, 1H), 1.94 (dd, $J = 6.8, 1.6$ Hz, 3H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 178.0, 150.0, 133.6, 100.3, 98.0, 18.4, -0.7; MS (EI, 70 eV) m/z 166.1 (M^+ , 16), 151.1 ($[\text{M} - \text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_9\text{H}_{14}\text{OSi}$ (M^+) 166.0814, found 166.0813.

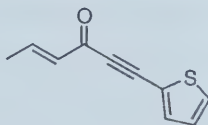
1-(2-Thienyl)hex-4-en-1-yn-3-ol (**198o**).



To a solution of 2-(2-thienyl)-ethynyltrimethylsilane (0.818 g, 4.53 mmol) in wet methanol (25 mL) was added potassium carbonate (ca. 0.2 eq), the mixture stirred for 30 min., ether and water added, the organic phase separated, washed with brine, dried and reduced under vacuo to give the corresponding terminal acetylene, 2-ethynyl-thiophene, as a yellow oil that was used in the next step without additional purification. To 2-ethynyl-thiophene (4.53 mmol) in diethyl ether at -78°C was

added *n*-BuLi (1.7 mL, 2.5 M in hexanes, 4.25 mmol). After stirring for 30 minutes, crotonaldehyde (0.267 g, 3.82 mmol, 0.300 mL) was added and stirring was continued for 2 h at $-78\text{ }^{\circ}\text{C}$. The reaction was quenched with sat. aq. NH_4Cl at $-78\text{ }^{\circ}\text{C}$, extracted with ether, and dried (Na_2SO_4). Column chromatography (CH_2Cl_2 /hexanes, 1:2) gave **198o** (0.548 g, 80%) as a yellow oil: $R_f = 0.37$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 3300, 3106, 3029, 2966, 2939, 2915, 2854, 2221, 1672, 1517, 1189 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.16 (m, 2H), 6.88 (m, 1H), 5.90 (m, 1H), 5.63 (m, 1H), 5.00 (m, 1H), 1.91 (m, 1H), 1.67 (m, 3H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 132.4, 130.3, 129.4, 127.6, 127.0, 122.7, 93.6, 80.0, 63.9, 18.2; MS (EI, 70 eV) m/z 178.0 (M^+ , 100); HRMS m/z calcd for $\text{C}_{10}\text{H}_{10}\text{OS}$ (M^+) 178.0452, found 178.0452.

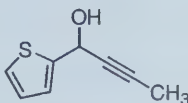
1-(2-Thienyl)hex-4-en-1-yn-3-one (**199o**).



(a) **PCC oxidation**: To **198o** (0.523 g, 2.93 mmol) in CH_2Cl_2 were sequentially added Celite (1 g), molecular sieves ($4\text{\AA}$, 1 g), and PCC (0.968 g, 4.40 mmol). The reaction mixture was stirred for 2 h at rt and the solution mixture was filtered through a plug (SiO_2 , CH_2Cl_2) to give **199o** (0.179 g, 35%) as a yellow oil: $R_f = 0.48$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 2189, 1647, 1620, 1513 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.44 (m, 2H), 7.19 (dq, $J = 15.7, 6.9$ Hz, 1H), 7.03 (dd, $J = 5.0, 3.8$ Hz, 1H), 6.21 (dq, $J = 15.7, 1.6$ Hz, 1H), 1.98 (dd, $J = 6.9, 1.6$ Hz, 3H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 177.8, 149.3, 136.2, 133.6, 131.1, 127.6, 119.9, 90.8, 84.9, 18.5; MS (EI, 70 eV) m/z 176.0 (M^+ , 100); HRMS m/z calcd for $\text{C}_{10}\text{H}_8\text{OS}$ (M^+) 176.0296, found 176.0297. Anal. Calcd for $\text{C}_{10}\text{H}_8\text{OS}$: C, 68.15; H, 4.58. Found C, 67.73; H, 4.67. (b) **Barium manganate oxidation**: To **198o** (0.434 g, 2.43 mmol) in CH_2Cl_2 (20 mL) was added 3 equivalents of barium manganate (2.078 g, 7.30 mmol). After stirring for 1h, the reaction mixture was filtered through Celite and the solvent was evaporated to give **199o** as a yellow oil (0.352 g, 82%).

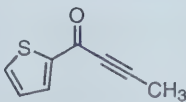
Compounds **198p–201q** were made by Sara Eisler and details about these compounds can be found in Chapter 2, ref. 1.

1-(2-Thienyl)but-2-yn-1-ol (198r).



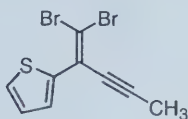
Propyne gas was bubbled through a solution of *n*-BuLi (2.5 M in hexanes, 26.7 mmol, 10.7 mL) in diethyl ether (60 mL) at $-78\text{ }^{\circ}\text{C}$. After stirring for 30 minutes, 2-thiophenecarboxaldehyde (2.00 g, 17.8 mmol, 1.7 mL) was added and stirring was continued for 2 h at $-78\text{ }^{\circ}\text{C}$. The reaction was quenched with sat. aq. NH_4Cl at $-78\text{ }^{\circ}\text{C}$, extracted with ether, and dried (Na_2SO_4). Column chromatography (hexanes/ CH_2Cl_2 2:1) gave **198r** (2.65 g, 98%) as a yellow oil: $R_f = 0.3$ (CH_2Cl_2); IR (CHCl_3 cast) 3372, 2228, 1435, 1380 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.28 (dd, $J = 5.3, 1.3$ Hz, 1H), 7.15 (dt, $J = 3.5, 1.0$ Hz, 1H), 6.97 (dd, $J = 5.3, 3.5$ Hz, 1H), 5.61 (s, 1H), 2.72 (d, $J = 6.5$ Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 145.4, 126.6, 125.7, 125.2, 82.6, 78.7, 60.3, 3.6; MS (EI, 70 eV) m/z 152.0 (M^+ , 100); HRMS m/z calcd for $\text{C}_8\text{H}_8\text{OS}$ (M^+) 152.0296, found 152.0296. Anal. Calcd for $\text{C}_8\text{H}_8\text{OS}$: C, 63.13; H, 5.30. Found C, 63.03; H, 5.28.

1-(2-Thienyl)but-2-yn-1-one (199r).



To **198r** (2.04 g, 13.4 mmol) in CH_2Cl_2 (60 mL) was added sequentially Celite (4.5 g), molecular sieves ($4\text{\AA}$, 4.5 g), and PCC (4.43 g, 20.1 mmol). The reaction mixture was stirred for 2 h at rt and the solution mixture was filtered through a plug (SiO_2 , CH_2Cl_2) to give **199r** (1.48 g, 73%) as a yellow oil: $R_f = 0.52$ (CH_2Cl_2); IR (CHCl_3 cast) 3102, 2237, 2198, 1620 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.91 (dd, $J = 4.0, 1.0$ Hz, 1H), 7.69 (dd, $J = 5.0, 1.0$ Hz, 1H), 7.15 (dd, $J = 5.0, 4.0$ Hz, 1H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.1, 145.0, 135.0, 134.9, 128.2, 91.0, 78.7, 4.3; EI HRMS m/z calcd for $\text{C}_8\text{H}_6\text{OS}$ (M^+) 150.0139, found 150.0140.

2-(1-Dibromomethylene-2-butynyl)thiophene (**200r**).



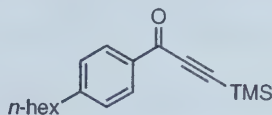
CBr_4 (0.240 g, 0.72 mmol) and PPh_3 (0.380 g, 1.43 mmol) were added to CH_2Cl_2 (40 mL) and the mixture stirred for 5 min at rt. Ketone **199r** (0.086 g, 0.57 mmol) in CH_2Cl_2 was added in one portion, the reaction stirred for 4 h, then concentrated to ca. 15 mL, hexanes (15 mL) was added, and the inhomogeneous mixture was filtered through Celite. Evaporation gave a yellow oil which was purified by passing through a plug of silica (hexanes) to give **200r** (0.029 g, 17%) as a yellow oil: $R_f = 0.97$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 3104, 2922, 2851, 2232 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.55 (dd, $J = 3.7, 1.2$ Hz, 1H), 7.35 (dd, $J = 5.2, 1.2$ Hz, 1H), 7.00 (dd, $J = 5.2, 3.7$ Hz, 1H), 2.05 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 139.2, 130.1, 127.3, 126.5, 124.6, 95.5, 94.8, 79.2, 4.7; MS (EI, 70 eV) m/z 303.9/305.9/307.9 (M^+ , 43/86/45); HRMS m/z calcd for $\text{C}_9\text{H}_6\text{S}^{79}\text{Br}_2/\text{C}_9\text{H}_6\text{S}^{79}\text{Br}^{81}\text{Br}/\text{C}_9\text{H}_6\text{S}^{81}\text{Br}_2$ (M^+) 303.8557/305.8536/307.8516, found 303.8562/305.8543/307.8522.

1-(2-Thienyl)-1,3-pentadiyne (**201r**).



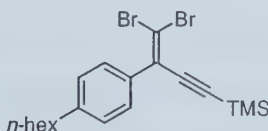
Dibromoolefin **200r** (76.6 mg, 0.250 mmol) was reacted with *n*-BuLi (0.12 mL, 2.5 M in hexanes, 0.30 mmol) as per the general procedure to give diyne **201r** (14.8 mg, 41%) as a colorless oil: $R_f = 0.5$ (hexanes); IR (CHCl_3 cast) 3105, 2912, 2850, 2236, 2150, 1426 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26 (dd, $J = 3.7, 1.2$ Hz, 1H), 7.25 (dd, $J = 5.2, 1.2$ Hz, 1H), 6.94 (dd, $J = 5.2, 3.7$ Hz, 1H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 133.9, 128.0, 127.0, 122.4, 82.6, 78.6, 67.2, 64.3, 4.8; EI HRMS m/z calcd for $\text{C}_9\text{H}_6\text{S}$ (M^+) 146.0190, found 146.0188.

1-(4-Hexylphenyl)-3-trimethylsilylpropynone (**202a**).



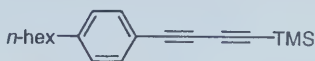
4-Hexylbenzoyl chloride (1.65 g, 7.3 mmol) was reacted with bis(trimethylsilyl)acetylene (1.25 g, 7.3 mmol) and AlCl_3 (0.97 g, 7.3 mmol) as per the general procedure, with more AlCl_3 (0.4 g, 3.0 mmol) being added until the reaction was deemed complete by TLC, to give ketone **202a** (1.88 g, 90%) as a greenish yellow oil: R_f = 0.76 (hexanes/ Et_2O 7:3); IR (CHCl_3 cast) 2958, 2929, 2153, 1644, 1255 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.02 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 2.64 (t, J = 7.7 Hz, 2H), 1.60 (m, 2H), 1.27 (m, 6H), 0.85 (m, 3H), 0.28 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 177.3, 150.1, 134.4, 129.7, 128.6, 101.0, 99.8, 36.1, 31.6, 30.9, 28.8, 22.5, 14.0, -0.7; MS (EI, 70 eV) m/z 286.2 (M^+ , 46), 271.2 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{18}\text{H}_{26}\text{OSi}$ (M^+) 286.1753, found 286.1756. Anal. Calcd for $\text{C}_{18}\text{H}_{26}\text{OSi}$: C, 75.46; H, 9.15. Found C, 75.32; H, 9.21.

[4,4-Dibromo-3-(4-hexylphenyl)buten-1-ynyl]trimethylsilane (**203a**).



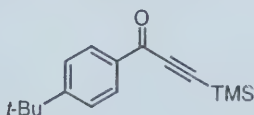
Ketone **202a** (1.00 g, 3.5 mmol) was reacted with CBr_4 (1.40 g, 4.2 mmol) and PPh_3 (2.40 g, 9.1 mmol) as per the general procedure to give **203a** (1.22 g, 79%) as a yellow oil: R_f = 0.70 (hexanes); IR (CHCl_3 cast) 3036, 2957, 2135, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.32 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 8.2 Hz, 2H), 2.57 (t, J = 7.8 Hz, 2H), 1.58 (m, 2H), 1.28 (m, 6H), 0.86 (m, 3H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 143.5, 134.9, 130.9, 128.4, 128.2, 103.8, 103.5, 99.7, 35.8, 31.6, 31.1, 29.0, 22.5, 14.0, -0.4; EI HRMS m/z calcd for $\text{C}_{19}\text{H}_{26}\text{Si}^{79}\text{Br}^{81}\text{Br}$ (M^+) 442.0150, found 442.0129. Anal. Calcd for $\text{C}_{19}\text{H}_{26}\text{SiBr}_2$: C, 51.59; H, 5.93. Found C, 51.87; H, 5.91.

[4-(4-*n*-Hexylphenyl)-1,3-butadiynyl]trimethylsilane (**204a**).



Dibromoolefin **203a** (170 mg, 0.384 mmol) was reacted with *n*-BuLi (0.16 mL, 2.5 M in hexanes, 0.40 mmol) as per the general procedure to give diyne **204a** (76.1 mg, 70%) as a bright yellow oil: R_f = 0.6 (hexanes); IR (CHCl₃ cast) 3029, 2958, 2204, 2103, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.35 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 2.56 (t, J = 7.8 Hz, 2H), 1.58 (m, 2H), 1.26 (m, 6H), 0.84 (m, 3H), 0.20 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 144.8, 132.7, 128.6, 118.5, 90.2, 88.1, 77.2, 73.6, 36.1, 31.7, 31.2, 29.0, 22.6, 14.1, -0.3; MS (EI, 70 eV) m/z 282.2 (M⁺, 65), 267.2 ([M - CH₃]⁺, 100); EI HRMS m/z calcd for C₁₉H₂₆Si (M⁺) 282.1804, found 282.1796.

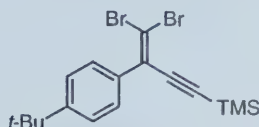
1-(4-*tert*-Butylphenyl)-3-trimethylsilylpropynone (**202b**).*



4-*tert*-Butylbenzoyl chloride (1.02 g, 5.19 mmol) was reacted with bis(trimethylsilyl)acetylene (0.88 g, 5.19 mmol) and AlCl₃ (0.69 g, 5.17 mmol) as per the general procedure, with more AlCl₃ (0.26 g, 2.0 mmol) being added until the reaction was deemed complete by TLC, to give ketone **202b** (1.04 g, 78%) as a yellow oil: R_f = 0.79 (hexanes/Et₂O 7:3); IR (CH₂Cl₂ cast) 2964, 2904, 2154, 1645, 1261 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 1.28 (s, 9H), 0.26 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 177.4, 158.2, 134.2, 129.7, 125.6, 101.1, 100.0, 35.3, 31.1, -0.6; MS (EI, 70 eV) m/z 258.1 (M⁺, 25), 243.1 ([M - CH₃]⁺, 100); HRMS m/z calcd for C₁₆H₂₂OSi (M⁺) 258.1440, found 258.1444.

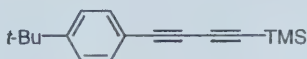
*Previously reported by: Suzuki, R.; Tsukuda, H.; Watanabe, N.; Kuwatani, Y.; Ueda, I. *Tetrahedron* **1998**, 54, 2477-2496.

[4,4-Dibromo-3-(4-*tert*-butylphenyl)buten-1-ynyl]trimethylsilane (203b).



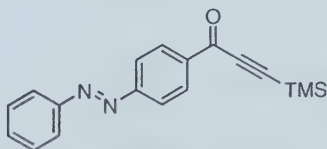
Ketone **202b** (0.25 g, 0.97 mmol) was reacted with CBr_4 (0.39 g, 1.2 mmol) and PPh_3 (0.66 g, 2.5 mmol) as per the general procedure to give **203b** (0.245 g, 61%) as a white solid: mp 69-70 °C; R_f = 0.75 (hexanes); IR (CH_2Cl_2 cast) 2962, 2183, 2134, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.38 (s, 4H), 1.36 (s, 9H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 151.7, 134.7, 130.9, 128.4, 125.2, 103.8, 103.6, 99.8, 31.3, -0.3; EI HRMS m/z calcd for $\text{C}_{17}\text{H}_{22}\text{Si}^{79}\text{Br}^{81}\text{Br}$ (M^+) 413.9837, found 413.9801.

[4-(4-*tert*-Butylphenyl)-1,3-butadiynyl]trimethylsilane (204b).



Dibromoolefin **203b** (152 mg, 0.367 mmol) was reacted with *n*-BuLi (0.15 mL, 2.5 M in hexanes, 0.38 mmol) as per the general procedure to give diyne **204b** (82.2 mg, 88%) as a yellow crystalline solid. Spectral data were consistent with those reported by: Wan, W. B.; Haley, M. M. *J. Org. Chem.* **2001**, 66, 3893–3901.

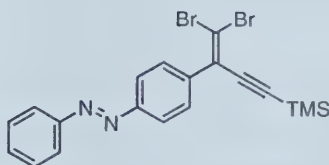
1-(4-Phenylazophenyl)-3-trimethylsilylpropynone (202c).



To a solution of 4-phenylazobenzoyl chloride (2.00 g, 8.17 mmol) in dry CH_2Cl_2 (80 mL) at 0 °C, bis(trimethylsilyl)acetylene (1.39 g, 8.17 mmol) was added, followed by slow addition of AlCl_3 (1.09 g, 8.17 mmol) as per the general procedure to give the ketone **202c** (1.07 g, 43%) as a red solid: mp 68-69 °C; R_f = 0.67 (hexanes/ CH_2Cl_2 1:1); IR (CH_2Cl_2 cast) 2956, 2159, 1635, 1249 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.28 (d, J = 8.8 Hz, 2H), 7.70 (m, 4H), 7.54 (m, 3H), 0.34 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.9, 155.7, 152.6, 137.8, 132.0, 130.8, 129.3, 123.3, 122.9, 101.4, 100.9,

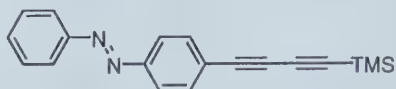
–0.6; MS (EI, 70 eV) m/z 306.1 (M^+ , 86), 77.0 ($C_6H_5^+$, 100); EI HRMS m/z calcd for $C_{18}H_{18}ON_2Si$ (M^+) 306.1188, found 306.1183. Anal. Calcd for $C_{18}H_{18}ON_2Si$: C, 70.55; H, 5.92; N, 9.14. Found C, 70.64; H, 5.70; N, 9.11.

[4-(1-Dibromomethylene-3-trimethylsilylprop-2-ynyl)phenyl]phenyldiazene (203c).



Ketone **202c** (0.448 g, 1.46 mmol) was reacted with $CBBr_4$ (0.75 g, 2.2 mmol) and PPh_3 (1.50 g, 5.66 mmol) as per the general procedure to give **203c** (0.560 g, 83%) as a bright orange solid: mp 92–94 °C; R_f = 0.57 (hexanes/ CH_2Cl_2 2:1); IR ($CHCl_3$ cast) 2958, 2132, 2028, 1250 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.93 (m, 4H), 7.62 (d, J = 8.8 Hz, 2H), 7.51 (m, 3H), 0.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 152.2, 140.1, 131.2, 130.3, 129.5, 129.1, 122.9, 122.8, 104.7, 103.0, 100.9, –0.4; EI HRMS m/z calcd for $C_{19}H_{18}N_2Si^{79}Br_2/C_{19}H_{18}N_2Si^{79}Br^{81}Br/C_{19}H_{18}N_2Si^{81}Br_2$ (M^+) 459.9606/461.9586/463.9565, found 459.9633/461.9585/463.9574. Anal. Calcd for $C_{19}H_{18}N_2SiBr_2$: C, 49.37; H, 3.93; N, 6.06. Found C, 49.76; H, 3.69; N, 5.91.

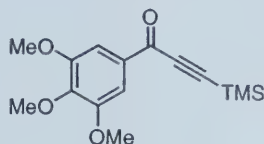
[4-(4-Trimethylsilyl-1,3-butadiynyl)phenyl]phenyldiazene (204c).



Dibromoolefin **203c** (170 mg, 0.369 mmol) was reacted with n -BuLi (0.15 mL, 2.5 M in hexanes, 0.38 mmol) as per the general procedure to give diyne **204c** (67.6 mg, 61%) as a red solid: mp 103–104 °C; R_f = 0.7 (hexanes/ CH_2Cl_2 2:1); IR (CH_2Cl_2 cast) 2960, 2202, 2102, 1404, 1278, 1253, 842 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 8.3, 1.8 Hz, 2H), 7.86 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 7.50 (m, 3H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 152.5, 152.3, 133.5, 131.4, 129.1, 123.9, 123.0, 122.9, 92.2, 87.7, 76.4, 76.4, –0.2; MS (EI, 70 eV) m/z 302.1 (M^+ , 89),

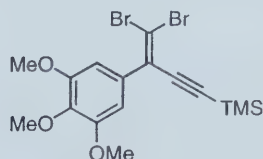
297.0 ($[M - C_6H_3N_2]^+$, 100); EI HRMS m/z calcd for $C_{19}H_{18}N_2Si$ (M^+): 302.1239, found 302.1245.

1-(3,4,5-Trimethoxyphenyl)-3-trimethylsilylpropynone (202d).



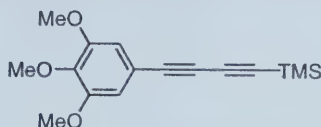
To a solution of 3,4,5-trimethoxybenzoyl chloride (0.47 g, 2.0 mmol) in dry CH_2Cl_2 at 0 °C, bis(trimethylsilyl)acetylene (0.35 g, 2.0 mmol) was added, followed by slow addition of $AlCl_3$ (0.27 g, 2.0 mmol) as per the general procedure to give the ketone **202d** (0.54 g, 91%) as a white solid: mp 54-55 °C; R_f = 0.39 (hexanes/ Et_2O 7:3); IR (CH_2Cl_2 cast) 2959, 2837, 2154, 1642, 1251 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.37(s, 2H), 3.87 (s, 3H), 3.86 (s, 6H), 0.26 (s, 9H); ^{13}C NMR (100 MHz, APT, $CDCl_3$) δ 176.7, 152.9, 143.3, 131.7, 106.9, 100.7, 100.2, 60.9, 56.1, -0.8; EI HRMS m/z calcd for $C_{15}H_{20}O_4Si$ (M^+) 292.1131, found 292.1132. Anal. Calcd for $C_{15}H_{20}O_4Si$: C, 61.61; H, 6.89. Found C, 61.58; H, 7.06.

[4,4-Dibromo-3-(3,4,5-trimethoxyphenyl)buten-1-ynyl]trimethylsilane (203d).



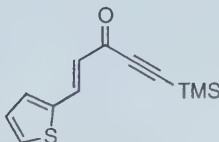
Ketone **202d** (0.19 g, 0.64 mmol) was reacted with CBr_4 (0.16 g, 0.48 mmol) and PPh_3 (0.44 g, 1.7 mmol) as per the general procedure to give **203d** (0.263 g, 91%) as a white solid: mp 48-49 °C; R_f = 0.2 (hexanes/ CH_2Cl_2 1:3); IR (microscope) 2958, 2836, 2154, 2139, 1247 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 6.64 (s, 2H), 3.83 (s, 3H), 3.82 (s, 6H), 0.20 (s, 9H); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 153.0, 138.3, 132.9, 130.8, 106.1, 104.4, 103.3, 100.1, 60.9, 56.2, -0.3; EI HRMS m/z calcd for $C_{16}H_{20}O_3Si^{79}Br^{81}Br$ (M^+) 447.9528, found 447.9557.

[4-(3,4,5-Trimethoxyphenyl)-1,3-butadiynyl]trimethylsilane (204d).



Dibromoolefin **203d** (255 mg, 0.569 mmol) was reacted with *n*-BuLi (0.27 mL, 2.5 M in hexanes, 0.68 mmol) as per the general procedure and purification by column chromatography (SiO₂, hexanes/CH₂Cl₂ 4:1) gave diyne **204d** (83.1 mg, 51%) as a yellow solid: mp 75-78 °C; *R_f* = 0.2 (hexanes/CH₂Cl₂ 1:1); IR (CHCl₃ cast) 2959, 2203, 2095, 1249, 1130 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.71 (s, 2H), 3.84 (s, 3H), 3.82 (s, 6H), 0.21 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 153.0, 140.0, 116.1, 109.9, 90.6, 87.7, 76.8, 73.3, 60.9, 56.1, -0.4; EI HRMS *m/z* calcd for C₁₆H₂₀O₃Si (M⁺) 288.1182, found 288.1179. Anal. Calcd for C₁₆H₂₀O₃Si: C, 66.63; H, 6.99. Found C, 66.73; H, 7.03.

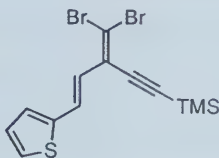
1-(2-Thienyl)-5-trimethylsilylpent-1-en-4-yn-3-one (202e).



To a solution of 3-(2-thienyl)acryloyl chloride (2.18 g, 12.6 mmol) in dry CH₂Cl₂ at 0 °C, bis(trimethylsilyl)acetylene (2.15 g, 12.6 mmol) was added, followed by slow addition of AlCl₃ (1.68 g, 12.6 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/CH₂Cl₂ 2:1) gave the ketone **202e** (1.82 g, 62%) as an orange oil: *R_f* = 0.65 (CH₂Cl₂); IR (CHCl₃ cast) 2960, 2156, 1622, 1583, 1421, 1240, 1185 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.89 (dd, *J* = 15.8, 0.7 Hz, 1H), 7.45 (dd, *J* = 4.8, 0.7 Hz, 1H), 7.34 (m, 1H), 7.07 (ddd, *J* = 4.8, 3.7, 1.3 Hz, 1H), 6.55 (dd, *J* = 15.8, 1.3 Hz, 1H), 0.27 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 177.1, 140.6, 139.2, 132.4, 130.2, 128.4, 126.9, 100.6, 98.4, -0.7; MS (EI, 70 eV) *m/z* 234.1 (M⁺, 80), 219.0 ([M - CH₃]⁺, 100); EI HRMS

m/z calcd for $C_{12}H_{14}OSSi$ (M^+) 234.0535, found 234.0533. Anal. Calcd for $C_{12}H_{14}OSiS$: C, 61.49; H, 6.02. Found C, 61.00; H, 6.23.

[3-Dibromomethylene-5-(2-thienyl)-pent-4-en-1-ynyl]trimethylsilane (**203e**).



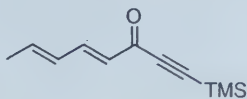
Ketone **202e** (0.877 g, 3.74 mmol) was reacted with CBr_4 (2.51 g, 7.48 mmol) and PPh_3 (3.97 g, 15.0 mmol) as per the general procedure to give **203e** (0.971 g, 67%) as a pale yellow crystalline solid: mp 67-69 °C; R_f = 0.48 (hexanes); IR ($CHCl_3$ cast) 2958, 2898, 2145, 1605, 1424, 1250 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 5.1 Hz, 1H), 7.25 (d, J = 15.4 Hz, 1H), 7.13 (d, J = 3.7 Hz, 1H), 7.00 (dd, J = 5.1, 3.7 Hz, 1H), 6.83 (d, J = 15.5 Hz, 1H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, APT, $CDCl_3$) δ 141.6, 128.9, 128.4, 128.0, 127.8, 126.1, 124.1, 104.9, 100.1, 99.5, -0.3; MS (EI, 70 eV) m/z 387.9/389.9/391.9 (M^+ , 10/19/10); HRMS m/z calcd for $C_{13}H_{14}SSi^{79}Br_2/C_{13}H_{14}SSi^{79}Br^{81}Br/C_{13}H_{14}SSi^{81}Br_2$ (M^+) 387.8952/389.8932/391.8911, found 387.8947/389.8930/391.8915. Anal. Calcd for $C_{13}H_{14}SiSBr_2$: C, 40.01; H, 3.62. Found C, 40.33; H, 3.81.

[6-(2-Thienyl)-hex-5-ene-1,3-diynyl]trimethylsilane (**204e**).



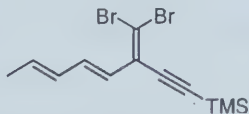
Dibromoolefin **203e** (679 mg, 1.74 mmol) was reacted with n -BuLi (0.84 mL, 2.5 M in hexanes, 2.1 mmol) as per the general procedure to give diyne **204e** (221 mg, 55%) as a yellow oil: R_f = 0.3 (hexanes); IR (CH_2Cl_2 cast) 2959, 2188, 2093, 1593, 1425, 1250 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 5.1 Hz, 1H), 7.16 (d, J = 15.9 Hz, 1H), 7.05 (d, J = 3.6 Hz, 1H), 6.99 (dd, J = 5.1, 3.6 Hz, 1H), 5.95 (d, J = 15.9 Hz, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, APT, $CDCl_3$) δ 140.8, 137.7, 128.0, 127.9, 126.4, 105.3, 91.6, 88.0, 76.7, 76.3, -0.4; MS (EI, 70 eV) m/z 230.1 (M^+ , 55), 215.0 ($[M - CH_3]^+$, 100); HRMS m/z calcd for $C_{13}H_{14}SSi$ (M^+) 230.0586, found 230.0586.

1-Trimethylsilyl-octa-4,6-dien-1-yn-3-one (**202f**).



Bis(trimethylsilyl)acetylene (0.976 g, 5.72 mmol) was added to sorbyl chloride (0.748 g, 5.72 mmol) in CH_2Cl_2 (16 mL) in an ice bath. The reaction mixture was stirred and anhydrous aluminium trichloride (0.763 g, 5.72 mmol) was slowly added. After stirring for 3 h at -5°C , the solution was poured into a mixture of 10% aq. HCl (5 mL) and ice (15 mL). The aqueous layer was extracted with diethyl ether (4 x 25 mL) and the combined organic phases were washed with saturated sodium hydrogencarbonate solution, followed by brine, and then dried over anhydrous MgSO_4 . The solvent was evaporated to give a yellow oil which was purified by column chromatography (hexanes/ CH_2Cl_2 2:1) to afford ketone **202f** (0.722 g, 66%) as a yellow oil: $R_f = 0.58$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 2962, 2155, 1625 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.38 (m, 1H), 6.26 (m, 2H), 6.09 (d, $J = 15.3$ Hz, 1H), 1.88 (d, $J = 5.1$ Hz, 3H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 178.2, 149.1, 142.4, 130.1, 129.6, 100.7, 97.9, 18.9, -0.7 ; MS (EI, 70 eV) m/z 192.1 (M^+ , 14), 177.1 ($[\text{M} - \text{CH}_3]^+$, 39); HRMS m/z calcd for $\text{C}_{11}\text{H}_{16}\text{OSi}$ (M^+) 192.0971, found 192.0963. Anal. Calcd for $\text{C}_{11}\text{H}_{16}\text{OSi}$: C, 68.69; H, 8.39. Found C, 68.26; H, 8.38.

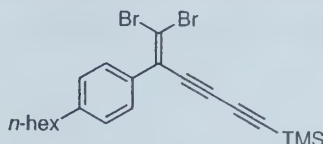
(3-Dibromomethylene-octa-4,6-dien-1-ynyl)trimethylsilane (**203f**).



CBr_4 (1.46 g, 4.36 mmol) and PPh_3 (2.31 g, 8.71 mmol) were added to CH_2Cl_2 (25 mL) and the mixture stirred for 5 min at rt. Ketone **202f** (0.419 g, 2.18 mmol) in CH_2Cl_2 (5 mL) was added in one portion. The reaction mixture was stirred for 4 h, concentrated to ca. 15 mL, hexanes (15 mL) added, and the inhomogeneous mixture was filtered through Celite. Evaporation gave a yellow oil which was purified by passing through a plug of silica (hexanes) to give **203f** (0.310 g, 41%) as a yellow oil: $R_f = 0.97$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 2959, 2924, 2852, 2145 cm^{-1} ; ^1H NMR (300

MHz, CDCl₃) δ 6.74 (dd, $J = 15.0, 10.6$ Hz, 1H), 6.33 (d, $J = 15.0$ Hz, 1H), 6.15 (m, 1H), 5.95 (m, 1H), 1.77 (d, $J = 6.7$ Hz, 3H), 0.23 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 136.8, 134.2, 131.0, 128.9, 125.7, 104.3, 99.8, 98.9, 18.5, -0.3; MS (EI, 70 eV) m/z 345.9/347.9/349.9 (M^+ , 10/20/10); HRMS m/z calcd for C₁₂H₁₆Si⁷⁹Br₂/C₁₂H₁₆Si⁷⁹Br⁸¹Br/ C₁₂H₁₆Si⁸¹Br₂ (M^+) 345.9388/347.9368/ 349.9347, found 345.9383/347.9363/349.9339.

[6,6-Dibromo-5-(4-*n*-hexylphenyl)hex-5-ene-1,3-diynyl]trimethylsilane (206a).



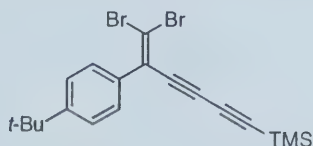
To a solution of 4-hexylbenzoyl chloride (0.456 g, 2.03 mmol) in dry CH₂Cl₂ (40 mL) at 0 °C, was added 1,4-bis(trimethylsilyl)-1,3-butadiyne (0.414 g, 2.13 mmol), followed by slow addition of AlCl₃ (0.325 g, 2.44 mmol). The reaction mixture was stirred for 3 h and worked up as per the general procedure. The resulting ketone **205a** was reacted overnight with CBr₄ (0.815 g, 2.43 mmol) and PPh₃ (1.38 g, 5.21 mmol). Then, more of the brominating mixture (0.20 g CBr₄ and 0.69 g PPh₃) was added. Work-up and purification by column chromatography (hexanes) gave dibromoolefin **206a** (0.202 g, 21%) as a yellow oil: $R_f = 0.69$ (hexanes); IR (CHCl₃ cast) 2956, 2927, 2855, 2167, 2092, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.26 (d, $J = 8.2$ Hz, 2H), 7.13 (d, $J = 8.2$ Hz, 2H), 2.56 (t, $J = 7.8$ Hz, 2H), 1.56 (m, 2H), 1.26 (m, 6H), 0.85 (m, 3H), 0.17 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 143.9, 134.4, 130.0, 128.5, 128.4, 102.1, 95.2, 87.5, 82.0, 75.2, 35.9, 31.8, 31.3, 29.1, 22.7, 14.2, -0.4; EI HRMS m/z calcd for C₂₁H₂₆Si⁷⁹Br₂/C₂₁H₂₆Si⁷⁹Br⁸¹Br/C₂₁H₂₆Si⁸¹Br₂ (M^+) 464.0171/466.0150/468.0130, found 464.0157/466.0138/468.0132. Anal. Calcd for C₂₁H₂₆SiBr₂: C, 54.09; H, 5.62. Found C, 54.41; H, 5.49.

[6-(4-*n*-Hexylphenyl)-1,3,5-hexatriynyl]trimethylsilane (207a).



Dibromoolefin **206a** (171 mg, 0.366 mmol) was reacted with *n*-BuLi (0.15 mL, 2.5 M in hexanes, 0.38 mmol) as per the general procedure to give triyne **207a** (46.4 mg, 41%) as a light yellow oil: R_f = 0.7 (hexanes); IR (CH₂Cl₂ cast) 3029, 2957, 2928, 2856, 2176, 2075, 1604, 1509, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.41 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.2 Hz, 2H), 2.59 (t, J = 7.8 Hz, 2H), 1.60 (m, 2H), 1.28 (m, 6H), 0.87 (m, 3H), 0.21 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 145.4, 133.1, 128.7, 117.9, 88.8, 88.2, 77.4, 73.8, 66.6, 61.9, 36.1, 31.7, 31.1, 28.9, 22.6, 14.1, -0.4; MS (EI, 70 eV) m/z 306.2 (M⁺, 96), 291.2 ([M - CH₃]⁺, 100); EI HRMS m/z calcd for C₂₁H₂₆Si (M⁺) 306.1804, found 306.1817. Anal. Calcd for C₂₁H₂₆Si: C, 82.29; H, 8.55. Found C, 81.82; H, 8.74.

[6,6-Dibromo-5-(4-*tert*-butylphenyl)hex-5-ene-1,3-diynyl]trimethylsilane (206b).



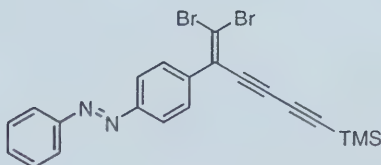
To a solution of 4-*tert*-butylbenzoyl chloride (0.503 g, 2.56 mmol) in dry CH₂Cl₂ (50 mL) at 0 °C, 1,4-bis(trimethylsilyl)-1,3-butadiyne (0.519 g, 2.67 mmol) was added, followed by slow addition of AlCl₃ (0.406 g, 3.04 mmol). The reaction mixture was stirred for 3 h and aqueous work-up as per the general procedure was carried out. The resulting ketone **205b** was reacted with CBr₄ (1.02 g, 3.04 mmol) and PPh₃ (1.73 g, 6.60 mmol) as per the general procedure and stirred overnight. Then, more of the brominating mixture (0.26 g CBr₄ and 0.87 g PPh₃) was added and the reaction mixture was heated. Work-up and purification by column chromatography (hexanes) gave dibromoolefin **206b** (0.269 g, 24%) as a yellow crystalline solid: mp 96-98 °C; R_f = 0.93 (hexanes/CH₂Cl₂ 1:1); IR (CHCl₃ cast) 2962, 2902, 2195, 2095, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.35 (m, 4H), 1.32 (s, 9H), 0.20 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 152.0, 134.2, 130.0, 128.3, 125.5, 102.1, 95.2, 87.5, 82.0, 75.2, 34.8, 31.3, -0.5; MS (EI, 70 eV) m/z 436.0/438.0/440.0 (M⁺, 40/79/40); HRMS m/z calcd for C₁₉H₂₂Si⁷⁹Br₂/C₁₉H₂₂Si⁷⁹Br⁸¹Br/C₁₉H₂₂Si⁸¹Br₂ (M⁺) 435.9858/437.9837/439.9817, found 435.9860/437.9833/439.9820.

[6-(4-*tert*-Butylphenyl)-1,3,5-hexatriynyl]trimethylsilane (207b).



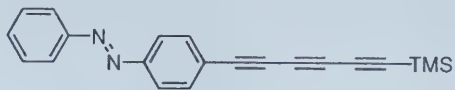
Dibromoolefin **206b** (80.6 mg, 0.184 mmol) was reacted with *n*-BuLi (0.08 mL, 2.5 M in hexanes, 0.20 mmol) as per the general procedure to give triyne **207b** (50.0 mg, 98%) as a yellow solid: mp 78-80 °C; R_f = 0.9 (hexanes/ CH_2Cl_2 2:1); IR (CHCl_3 cast) 2962, 2903, 2181, 2169, 2075, 1652, 1599, 1504, 1462, 1407 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.44 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.7 Hz, 2H), 1.30 (s, 9H), 0.21 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 153.5, 132.9, 125.6, 117.7, 88.8, 88.2, 77.3, 73.8, 66.6, 61.9, 35.0, 31.1, -0.4; MS (EI, 70 eV) m/z 278.1 (M^+ , 49), 263.1 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{19}\text{H}_{22}\text{Si}$ (M^+) 278.1491, found 278.1497.

[4-(1-Dibromomethylene-5-trimethylsilylpenta-2,4-diynyl)phenyl]phenyldiazene (206c).



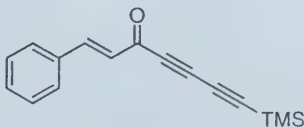
To a solution of 4-phenylazobenzoyl chloride (0.874 g, 3.57 mmol) in dry CH_2Cl_2 (90 mL) at 0 °C, 1,4-bis(trimethylsilyl)-1,3-butadiyne (0.698 g, 3.59 mmol) was added, followed by slow addition of AlCl_3 (0.48 g, 3.60 mmol). The reaction mixture was stirred for 3 h and aqueous work-up as per the general procedure was carried out. The resulting ketone **205c** was reacted with CBr_4 (1.44 g, 4.30 mmol) and PPh_3 (2.46 g, 9.29 mmol) as per the general procedure to give dibromoolefin **206c** (0.136 g, 8%) as a bright orange solid: mp 94-95 °C; R_f = 0.13 (hexanes); IR (CH_2Cl_2 cast) 3065, 2960, 2093, 2067, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.91 (m, 4H), 7.52 (m, 5H), 0.16 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 152.6, 152.3, 139.4, 131.3, 129.4, 129.1, 122.93, 122.90, 103.4, 95.9, 88.0, 87.2, 85.9, 74.5, -0.6; EI HRMS m/z calcd for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{Si}^{79}\text{Br}^{81}\text{Br}$ (M^+) 485.9586, found 485.9580.

[4-(6-Trimethylsilyl-1,3,5-hexatriynyl)phenyl]phenyldiazene (207c).



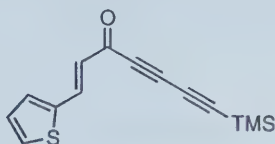
Dibromoolefin **206c** (54.7 mg, 0.113 mmol) was reacted with *n*-BuLi (0.04 mL, 2.5 M in hexanes, 0.10 mmol) as per the general procedure to give triyne **207c** (16.8 mg, 46%) as a bright orange solid, a mixture of *E*- and *Z*- isomers: mp 88-89 °C; R_f = 0.6 (hexanes/CH₂Cl₂ 4:1); IR (CH₂Cl₂ cast) 2959, 2167, 2075, 1248, 843 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91 (dd, J = 8.3, 2.1 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 7.50 (m, 3H), 0.23 (s, 9H); ¹³C NMR (75 MHz, APT, CDCl₃) δ (major isomer) 152.7, 152.6, 134.0, 131.6, 129.2, 123.3, 123.1, 123.0, 89.9, 88.0, 77.3, 76.5, 68.1, 61.4, -0.5; MS (EI, 70 eV) m/z 326.1 (M⁺, 93), 221.1 ([M - C₆H₅N₂]⁺, 100); EI HRMS m/z calcd for C₂₁H₁₈N₂Si (M⁺) 326.1239, found 326.1241.

1-Phenyl-7-trimethylsilyl-hept-1-ene-4,6-diyn-3-one (205d).



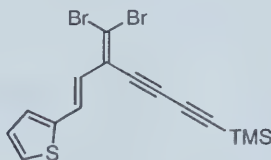
To a solution of cinnamoyl chloride (0.779 g, 4.63 mmol) in dry CH₂Cl₂ (40 mL) at 0 °C, 1,4-bis(trimethylsilyl)-1,3-butadiyne (1.00 g, 5.14 mmol) was added, followed by slow addition of AlCl₃ (0.617 g, 4.63 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/CH₂Cl₂ 2:1) gave the ketone **205d** (0.528 g, 45%) as a pale yellow solid: mp 60-61 °C; R_f = 0.69 (CH₂Cl₂); IR (CHCl₃ cast) 2961, 2209, 2097, 1630, 1449 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, J = 16.2 Hz, 1H), 7.58 (m, 2H), 7.43 (m, 3H), 6.79 (d, J = 16.2 Hz, 1H), 0.26 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 176.8, 149.4, 133.8, 131.4, 129.1, 128.7, 128.3, 96.5, 86.0, 75.6, 72.2, -0.7. MS (EI, 70 eV) m/z 252.1 (M⁺, 98), 237.1 ([M - CH₃]⁺, 100); EI HRMS m/z calcd for C₁₆H₁₆OSi (M⁺) 252.0971, found 252.0967. Anal. Calcd for C₁₆H₁₆OSi: C, 76.14; H, 6.39. Found C, 76.17; H, 6.31.

1-(2-Thienyl)-7-trimethylsilyl-hept-1-ene-4,6-diyne-3-one (205e).



To a solution of 3-(2-thienyl)acryloyl chloride (1.10 g, 6.38 mmol) in dry CH_2Cl_2 (30 mL) at 0 °C, 1,4-bis(trimethylsilyl)-1,3-butadiyne (1.24 g, 6.38 mmol) was added, followed by slow addition of AlCl_3 (0.85 g, 6.38 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/ CH_2Cl_2 2:1) gave ketone **205e** (1.13 g, 69%) as an orange oil: R_f = 0.67 (CH_2Cl_2); IR (CHCl_3 cast) 2959, 2925, 2853, 2208, 2098, 1623, 1582, 1512, 1253 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.88 (bd, J = 15.8 Hz, 1H), 7.48 (bd, J = 5.1 Hz, 1H), 7.38 (m, 1H), 7.10 (ddd, J = 5.3, 3.7, 1.1 Hz, 1H), 6.58 (dd, J = 15.8, 2.2 Hz, 1H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 176.0, 141.3, 139.1, 132.8, 130.7, 128.6, 127.1, 96.4, 86.0, 75.4, 72.2, -0.7; MS (EI, 70 eV) m/z 258.1 (M^+ , 31), 243.0 ($[\text{M} - \text{CH}_3]^+$, 54); HRMS m/z calcd for $\text{C}_{12}\text{H}_{14}\text{OSSi}$ (M^+) 258.0535, found 258.0532. Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{OSiS}$: C, 65.07; H, 5.46. Found C, 64.98; H, 5.28.

[5-Dibromomethylene-7-(2-thienyl)hept-6-ene-1,3-diynyl]trimethylsilane (206e).



Ketone **205e** (0.429 g, 1.66 mmol) was reacted with CBr_4 (1.11 g, 3.32 mmol) and PPh_3 (1.76 g, 6.65 mmol) as per the general procedure to give **206e** (0.517 g, 75%) as a pale yellow solid upon refrigeration: mp 94-95 °C; R_f = 0.48 (hexanes); IR (CH_2Cl_2 cast) 2958, 2924, 2852, 2227, 2104, 1606, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26 (d, J = 5.0 Hz, 1H), 7.24 (d, J = 15.5 Hz, 1H), 7.16 (d, J = 3.6 Hz, 1H), 7.00 (dd, J = 5.0, 3.6 Hz, 1H), 6.80 (d, J = 15.5 Hz, 1H), 0.25 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 141.3, 129.0, 128.3, 127.9, 127.3, 126.3, 123.9, 102.0, 94.3, 87.1, 82.5, 71.4, -0.5; MS (EI, 70 eV) m/z 411.9/413.9/415.9 (M^+ , 15/32/18); HRMS m/z

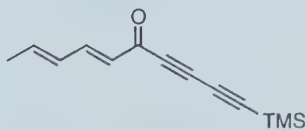
calcd for $C_{15}H_{14}SSi^{79}Br_2/C_{15}H_{14}SSi^{79}Br^{81}Br/C_{15}H_{14}SSi^{81}Br_2$ (M^+) 411.8952/413.8932/415.8911, found 411.8945/413.8926/415.8903. Anal. Calcd for $C_{15}H_{14}SSiBr_2$: C, 43.49; H, 3.41; S, 7.74. Found C, 43.65; H, 3.36; S, 7.51.

[8-(2-Thienyl)-oct-7-ene-1,3,5-triynyl]trimethylsilane (207e).



Dibromoolefin **206e** (459 mg, 1.11 mmol) was reacted with *n*-BuLi (0.53 mL, 2.5 M in hexanes, 1.3 mmol) as per the general procedure to give triyne **207e** (209 mg, 74%) as a yellow solid: mp 55-56 °C; R_f = 0.3 (hexanes); IR (CH_2Cl_2 cast) 2959, 2898, 2161, 2083, 2061, 1589, 1425, 1311, 1288, 1250 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 5.7 Hz, 1H), 7.23 (d, J = 15.6 Hz, 1H), 7.07 (d, J = 3.6 Hz, 1H), 7.00 (dd, J = 5.7, 3.6 Hz, 1H), 5.95 (d, J = 15.9 Hz, 1H), 0.20 (s, 9H); ^{13}C NMR (100 MHz, APT, $CDCl_3$) δ 140.6, 139.0, 128.5, 128.0, 126.9, 104.7, 89.6, 88.1, 76.9, 76.5, 67.8, 61.8, -0.5; MS (EI, 70 eV) m/z 254.1 (M^+ , 80), 239.0 ($[M - CH_3]^+$, 100); EI HRMS m/z calcd for $C_{15}H_{14}SSi$ (M^+) 254.0586, found 254.0590.

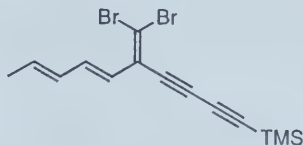
1-Trimethylsilyl-deca-6,8-diene-1,3-diyn-5-one (205f).



1,4-Bis(trimethylsilyl)-1,3-butadiyne (0.301 g, 1.54 mmol) was added to sorbyl chloride (0.202 g, 1.54 mmol) in CH_2Cl_2 (20 mL) cooled in an ice bath. The reaction mixture was stirred and anhydrous aluminium trichloride (0.206 g, 1.54 mmol) was slowly added. After 3 h of continuous stirring at 0-5 °C, the solution was poured into a mixture of 10% aq. HCl (5 mL) and ice (15 mL). The aqueous layer was extracted with diethyl ether (4 x 25 mL) and the combined organic phase was washed with saturated sodium hydrogencarbonate solution, followed by brine, and then dried over anhydrous $MgSO_4$. The solvent was evaporated to give a yellow oil which was purified by column chromatography (hexanes/ CH_2Cl_2 2:1) to afford ketone **205f** (0.217 g, 65%) as a yellow oil: R_f = 0.72 (CH_2Cl_2); IR (CH_2Cl_2 cast) 2209, 2097, 1621 cm^{-1} ;

^1H NMR (300 MHz, CDCl_3) δ 7.36 (dd, $J = 15.6, 10.1$ Hz, 1H), 6.28 (m, 2H), 6.10 (d, $J = 15.6$ Hz, 1H), 1.88 (d, $J = 5.7$ Hz, 3H), 0.21 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 177.0, 149.8, 143.3, 130.1, 129.7, 96.0, 86.1, 75.1, 72.4, 19.1, -0.7 ; MS (EI, 70 eV) m/z 216.1 (M^+ , 63), 201.1 ($[\text{M} - \text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{13}\text{H}_{16}\text{OSi}$ (M^+) 216.0971, found 216.0971.

(5-Dibromomethylene-deca-6,8-diene-1,3-diynyl)trimethylsilane (206f).



CBr_4 (0.324 g, 0.97 mmol) and PPh_3 (0.513 g, 1.94 mmol) were added to CH_2Cl_2 (30 mL) and the mixture stirred for 5 min at rt. Ketone **205f** (0.168 g, 0.77 mmol) in CH_2Cl_2 was added in one portion. The reaction mixture was stirred and the mixture was monitored by TLC. After 1 h, another equivalent of the brominating agent was added. After 4 h, the solution was concentrated to ca. 15 mL, hexanes (15 mL) was added, and the inhomogeneous mixture filtered through Celite. Evaporation gave a yellow oil which was purified by passing through a plug of silica (hexanes) to give **206f** (0.116 g, 40%) as a reddish-orange oil: $R_f = 0.97$ (CH_2Cl_2); IR (CHCl_3 cast) 2960, 2257, 2103, 1717, 1251 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.68 (dd, $J = 15.1, 10.4$ Hz, 1H), 6.30 (d, $J = 15.1$, 1H), 6.13 (m, 1H), 5.99 (m, 1H), 1.76 (d, $J = 6.6$ Hz, 3H), 0.20 (s, 9H); ^{13}C NMR (125 MHz, APT, CDCl_3) δ 137.0, 135.0, 131.0, 127.9, 125.6, 101.0, 94.0, 87.3, 82.2, 71.9, 18.7, -0.4 ; MS (EI, 70 eV) m/z 369.9/371.9/373.9 (M^+ , 12/26/14); HRMS m/z calcd for $\text{C}_{14}\text{H}_{16}\text{Si}^{79}\text{Br}_2/\text{C}_{14}\text{H}_{16}\text{S}^{79}\text{Br}^{81}\text{Br}/\text{C}_{14}\text{H}_{16}\text{S}^{81}\text{Br}_2$ (M^+) 369.9388/371.9368/373.9347, found 369.9348/371.9329/373.9304.

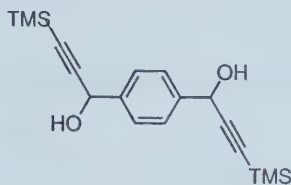
(Undeca-7,9-diene-1,3,5-triynyl)trimethylsilane (207f).



Dibromoolefin **206f** (104 mg, 0.279 mmol) was reacted with *n*-BuLi (0.13 mL, 2.5 M in hexanes, 0.34 mmol) as per the general procedure to give diyne **207f** (45.0 mg, 76%) as a pale yellow solid: mp 48-49 $^{\circ}\text{C}$; $R_f = 0.5$ (hexanes); IR (CHCl_3 cast) 2958,

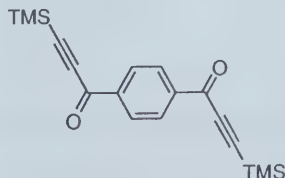
2924, 2853, 2162, 2074 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.74 (dd, $J = 15.6, 10.8$ Hz, 1H), 6.11 (dd, $J = 14.7, 10.8$ Hz, 1H), 5.90 (dq, $J = 14.7, 6.3$ Hz, 1H), 5.46 (d, $J = 15.6$ Hz, 1H), 1.79 (d, $J = 6.3$ Hz, 3H), 0.18 (s, 9H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 147.4, 135.9, 130.9, 106.3, 89.2, 88.3, 77.2, 76.0, 67.3, 62.0, 18.6, -0.4 ; MS (EI, 70 eV) m/z 212.1 (M^+ , 96), 197.1 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{14}\text{H}_{16}\text{Si}$ (M^+) 212.1021, found 212.1019.

1,4-Bis(1-hydroxy-3-trimethylsilylprop-2-ynyl)benzene **208**.



To (trimethylsilyl)acetylene (9.42 g, 94.0 mmol) in diethyl ether (150 mL) at -78°C was added $n\text{-BuLi}$ (32.9 mL, 2.5 M in hexanes, 82.2 mmol). After stirring for 0.5 h, a solution of terephthalaldehyde (5.25 g, 39.1 mmol) in THF (45 mL) was added and the reaction mixture was stirred at -78°C for 3 h. The general work-up procedure was followed to give **208** (11.41 g, 88%), presumably a mixture of stereoisomers, as a white solid: mp $117\text{--}119^\circ\text{C}$; $R_f = 0.16$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 3334, 2960, 2899, 2174, 1612, 1420, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.53 (s, 4H), 5.44 (d, $J = 6.1$ Hz, 2H), 2.34 (d, $J = 6.1$ Hz, 2H), 0.19 (s, 18H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 140.4, 126.9, 104.8, -91.7 , 64.6, -0.2 ; MS (EI, 70 eV) m/z 330.1 (M^+ , 9), 203.1 ($[\text{C}_{12}\text{H}_{15}\text{OSi}]^+$, 100); HRMS m/z calcd for $\text{C}_{18}\text{H}_{26}\text{O}_2\text{Si}_2$ (M^+) 330.1471, found 330.1472.

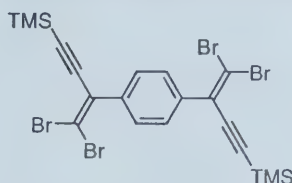
3-Trimethylsilyl-1-[4-(3-trimethylsilylpropynoyl)phenyl]propynone **209**.*



To **208** (4.84 g, 14.7 mmol) in CH_2Cl_2 (150 mL) was added sequentially Celite (11.3 g), molecular sieves ($4\text{\AA}$, 11.3 g), and PCC (11.28 g, 51.3 mmol). The reaction

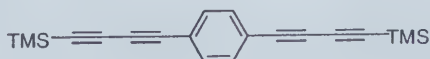
mixture was stirred for 2 h at rt and the solution mixture was filtered through a plug (SiO_2 , CH_2Cl_2) to give **209** (3.58 g, 75%) as a white fluffy solid: mp 143-144 °C; R_f = 0.80 (CH_2Cl_2); IR (CH_2Cl_2 cast) 2961, 2157, 1643, 1262, 1245 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.22 (s, 4H), 0.32 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 140.1, 129.7, 102.3, 100.6, -0.7; MS (EI, 70 eV) m/z 326.1 (M^+ , 42), 311.1 ($[\text{M}-\text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{18}\text{H}_{22}\text{O}_2\text{Si}_2$ (M^+) 326.1174, found 326.1157. Anal. Calcd for $\text{C}_{18}\text{H}_{22}\text{O}_2\text{Si}_2$: C, 66.21; H, 6.79. Found C, 66.16; H, 6.81. *Previously reported by: Walton, D. R. M.; Waugh, F. *J. Organomet. Chem.* **1972**, 37, 45-56.

1,4-Bis(1-dibromomethylene-3-trimethylsilylprop-2-ynyl)benzene **210**.



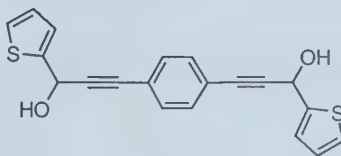
CBr_4 (6.65 g, 19.9 mmol) and PPh_3 (10.52 g, 39.7 mmol) were added to CH_2Cl_2 (150 mL) and the mixture stirred for 5 min at rt. Diketone **209** (3.24 g, 9.93 mmol) in CH_2Cl_2 was added in one portion and reacted as per the general procedure to give **210** (4.79 g, 76%) as a pale yellow solid: mp 107-108 °C; R_f = 0.85 (CH_2Cl_2); IR (CHCl_3 cast) 2959, 2898, 2135, 1400, 1250 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.45 (s, 4H), 0.21 (s, 18H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 137.7, 130.3, 128.6, 104.4, 103.2, 100.7, -0.4; MS (EI, 70 eV) m/z 633.8/635.8/637.8/639.8/641.8 (M^+ , 23/78/100/84/30); HRMS m/z calcd for $\text{C}_{20}\text{H}_{22}\text{Si}_2^{79}\text{Br}_4/\text{C}_{20}\text{H}_{22}\text{Si}_2^{79}\text{Br}_3^{81}\text{Br}/\text{C}_{20}\text{H}_{22}\text{Si}_2^{79}\text{Br}_2^{81}\text{Br}_2/\text{C}_{20}\text{H}_{22}\text{Si}_2^{79}\text{Br}^{81}\text{Br}_3/\text{C}_{20}\text{H}_{22}\text{Si}_2^{81}\text{Br}_4$ (M^+) 633.7994/635.7973/637.7953/639.7932/641.7911, found 633.7990/635.7975/637.7959/639.7944/641.7922. Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{Si}_2\text{Br}_4$: C, 37.64; H, 3.48. Found C, 37.66; H, 3.34.

1,4-Bis(4-trimethylsilyl-1,3-butadiynyl)benzene (**211**).



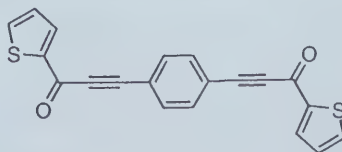
Dibromoolefin **210** (4.12 g, 6.46 mmol) was reacted with *n*-BuLi (6.2 mL, 2.5 M in hexanes, 15.5 mmol) as per the general procedure to give tetrayne **211** (1.79 g, 87%) as colorless crystals: mp 187-188 °C; R_f = 0.4 (hexanes); IR (CHCl₃ cast) 2957, 2209, 2105, 1400 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.40 (s, 4H), 0.21 (s, 18H); ¹³C NMR (100 MHz, CDCl₃) δ 132.6, 122.3, 92.4, 87.5, 76.7, 75.9, -0.5; MS (EI, 70 eV) m/z 318.1 (M⁺, 75), 303.1 ([M – CH₃]⁺, 100); EI HRMS m/z calcd for C₂₀H₂₂Si₂ (M⁺) 318.1260, found 318.1261. Anal. Calcd for C₂₀H₂₂Si₂: C, 75.40; H, 6.96. Found C, 75.01; H, 6.89.

1,4-Bis[3-hydroxy-3-(2-thienyl)propynyl]benzene (S1).



To 1,4-diethynylbenzene (0.45 g, 3.6 mmol) in diethyl ether at -78 °C was added *n*-BuLi (2.85 mL, 2.5 M in hexanes, 7.13 mmol). After stirring for 1 h, 2-thiophene carboxaldehyde (0.733 g, 6.41 mmol) was added and the reaction mixture was stirred at -78 °C for 3 h. The general work-up procedure was followed to give 1,4-bis[3-hydroxy-3-(2-thienyl)propynyl]benzene, **S1**, (0.868 g, 76%) as a tan solid: mp 92-94 °C; R_f = 0.2 (CH₂Cl₂); IR (CHCl₃ cast) 3334, 3105, 2229, 1506 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.41 (s, 4H), 7.30 (m, 2H), 7.22 (m, 2H), 6.97 (dd, J = 5.1, 3.5 Hz, 2H), 5.86 (d, J = 6.8 Hz, 2H), 2.35 (d, J = 6.8 Hz, 2H); ¹³C NMR (75 MHz, APT, CDCl₃) δ 144.4, 131.7, 126.9, 126.2, 125.7, 122.6, 90.1, 85.5, 60.8; EI HRMS m/z calcd for C₂₀H₁₄O₂S₂ (M⁺) 350.0435, found 350.0421.

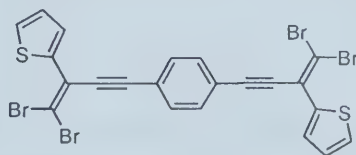
1,4-Bis[3-oxo-3-(2-thienyl)propynyl]benzene S2.



The bis-alcohol **S1** (0.228 g, 0.65 mmol) was reacted with barium manganate (1.60 g, 6.24 mmol) as per the general procedure to give 1,4-bis[3-oxo-3-(2-

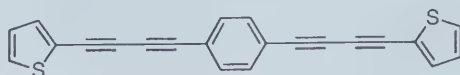
thienyl)propynyl]benzene (0.209 g, 93%) as a tan solid: decomposition at 202 °C; $R_f = 0.6$ (CH_2Cl_2 /hexanes/ Et_2O 5:3:1); IR (CH_2Cl_2 cast) 3097, 2200, 1622 cm^{-1} ; ^1H NMR (300 MHz, CD_2Cl_2) δ 8.03 (dd, $J = 3.8, 1.2$ Hz, 2H), 7.80 (dd, $J = 4.7, 1.2$ Hz, 2H), 7.24 (dd, $J = 4.7, 3.8$ Hz, 4H), 7.24 (m, 2H); ^{13}C NMR (75 MHz, APT, CD_2Cl_2) δ 169.5, 151.6, 136.0, 135.8, 133.5, 128.9, 122.7, 89.9, 88.7; EI HRMS m/z calcd for $\text{C}_{20}\text{H}_{10}\text{O}_2\text{S}_2$ (M^+) 346.0122, found 346.0110. Anal. Calcd for $\text{C}_{20}\text{H}_{10}\text{O}_2\text{S}_2$: C, 69.34; H, 2.91. Found C, 69.46; H, 2.94. **With PCC:** To **S1** (0.626 g, 1.71 mmol) in CH_2Cl_2 (70 mL) was added sequentially celite (1 g), molecular sieves (4Å, 1 g), and PCC (0.92 g, 4.3 mmol). The reaction mixture was stirred for 2 h at rt and the solution mixture was filtered through a plug (SiO_2 , CH_2Cl_2) to give **S2** (0.44 g, 74%).

1,4-Bis[3-dibromomethylene-3-(2-thienyl)propynyl]benzene **212**.



CBr_4 (1.4 g, 4.2 mmol) and PPh_3 (2.21 g, 8.5 mmol) were added to CH_2Cl_2 (150 mL) and the mixture stirred for 5 min at rt. Diketone **S2** (0.44 g, 1.3 mmol) in CH_2Cl_2 (10 mL) was added in one portion and reacted as per the general procedure to give **212** (0.281 g, 33%) as a pale yellow solid: mp 128-129 °C; $R_f = 0.63$ (hexanes/ Et_2O 4:1); IR (CH_2Cl_2 cast) 3100, 2207, 1508, 1489, 1420, 1404, 1343 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (m, 2H), 7.48 (s, 4H), 7.39 (m, 2H), 7.03 (m, 2H); ^{13}C NMR (75 MHz, APT, CDCl_3) δ 138.5, 131.5, 130.3, 127.7, 126.8, 124.2, 123.0, 97.3, 96.3, 90.6; EI HRMS m/z calcd for $\text{C}_{22}\text{H}_{10}\text{S}_2^{79}\text{Br}_2^{81}\text{Br}_2$ (M^+) 657.6917, found 657.6862.

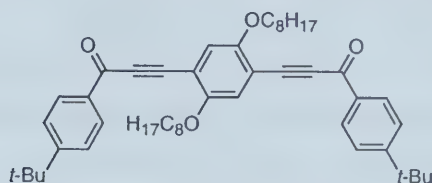
1,4-Bis[4-(2-thienyl)-1,3-butadiynyl]benzene (**214**).



The bis(dibromoolefin) **212** (37.6 mg, 0.057 mmol) was stirred in 7 mL dry hexanes at -78 °C and $n\text{-BuLi}$ (0.24 mL, 2.5 M in hexanes, 1.4 mmol) was added. The heterogeneous mixture was then warmed to about -10 °C for several minutes and then

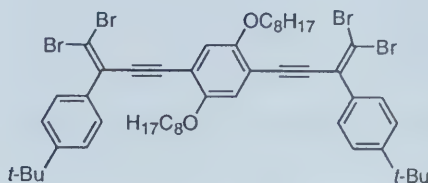
cooled to $-78\text{ }^{\circ}\text{C}$ before workup. Addition of CH_2Cl_2 was required to solubilize the product for work-up. Recrystallization (hexanes/ CH_2Cl_2) yielded **214** (4.5 mg, 24%) as a shiny light-brown solid: mp $261\text{ }^{\circ}\text{C}$ (decomp), $R_f = 0.7$ (hexanes/ CH_2Cl_2 1:1); IR (microscope) $3101, 2202, 2143, 1663\text{ cm}^{-1}$; ^1H NMR (400 MHz, CD_2Cl_2) δ 7.48 (s, 4H), 7.37 (d, $J = 4.4\text{ Hz}$, 4H), 7.01 (m, 2H); ^{13}C NMR (100 MHz, APT, CD_2Cl_2) δ 135.2, 132.8, 129.7, 127.7, 122.9, 121.9, 83.2, 77.8, 76.4, 76.3; EI HRMS m/z calcd for $\text{C}_{22}\text{H}_{10}\text{S}_2$ (M^+) 338.0224, found 338.0220.

1,4-Bis[3-(4-*tert*-butylphenyl)-3-oxopropynyl]-2,5-bis(octyloxy)benzene **S3**.



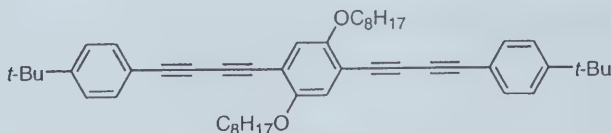
To a solution of *tert*-butylbenzoyl chloride (0.274 g, 1.40 mmol) in dry CH_2Cl_2 (10 mL) at $0\text{ }^{\circ}\text{C}$, was added 1,4-bis(trimethylsilylacetylene)-2,5-octyloxybenzene (0.368 g, 0.698 mmol), followed by slow addition of AlCl_3 (0.200 g, 1.54 mmol). The reaction was stirred for 3 h and aqueous work-up as per the general procedure was carried out. The crude product was rinsed with hexanes and filtered to give **S3**, (0.214 g, 44%) an orange waxy solid: mp $113\text{--}115\text{ }^{\circ}\text{C}$; $R_f = 0.52$ (hexanes/ EtOAc 4:1); IR (CH_2Cl_2 cast) $2955, 2926, 2854, 2193, 1638, 1603, 1566, 1499, 1270\text{ cm}^{-1}$; ^1H NMR (400 MHz, CDCl_3) δ 8.24 (d, $J = 8.4\text{ Hz}$, 4H), 7.50 (d, $J = 8.4\text{ Hz}$, 4H), 7.16 (s, 2H), 4.05 (t, $J = 6.4\text{ Hz}$, 4H), 1.92 (m, 4H), 1.51 (m, 4H), 1.35 (s, 18H), 1.24 (m, 16H), 0.84 (m, 6H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 177.5, 158.1, 155.0, 134.5, 129.8, 125.5, 117.5, 113.2, 92.8, 88.6, 69.5, 35.3, 31.8, 31.0, 29.5, 29.4, 29.2, 26.0, 22.6, 14.0; MS (EI, 70 eV) m/z 702.5 (M^+ , 34), 161.1 ($[\text{M} - \text{C}_{37}\text{H}_{49}\text{O}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{48}\text{H}_{62}\text{O}_4$ (M^+) 702.4648, found 702.4644.

1,4-Bis[3-(4-*tert*-butylphenyl)-3-dibromomethylenepropynyl]-2,5-bis(octyloxy)benzene **213.**



To a solution of CBr_4 (0.190 g, 0.572 mmol) and PPh_3 (0.300 g, 1.14 mmol) in acetonitrile (18 mL) was added a solution of the diketone precursor **S3** (0.996 g, 1.42 mmol) in CH_2Cl_2 (8 mL). The mixture was stirred and monitored by TLC. More brominating solution mixture of CBr_4 (0.190 g, 0.572 mmol) and PPh_3 (0.190 g, 1.14 mmol) was added and the reaction mixture was stirred until judged complete by TLC analysis. The reaction was worked-up as per the general procedure and the crude compound was purified by passing a plug of silica (hexanes/ CH_2Cl_2 4:1) to give **213** (245 mg, 17%) as a yellow solid: mp 108-109 °C; R_f = 0.75 (hexanes/EtOAc 19:1); IR (CH_2Cl_2 cast) 2955, 2924, 2855, 2196, 1495, 1415, 1221 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, J = 8.6 Hz, 4H), 7.38 (d, J = 8.6 Hz, 4H), 6.84 (s, 2H), 3.89 (t, J = 6.6 Hz, 4H), 1.71 (m, 4H), 1.42 (m, 4H), 1.32 (m, 18H), 1.31 (m, 16H), 0.87 (m, 6H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 153.7, 151.6, 134.9, 131.0, 128.4, 125.1, 116.4, 113.8, 98.1, 94.5, 94.0, 69.5, 34.7, 31.8, 31.2, 29.4, 29.3, 29.2, 26.0, 22.6, 14.1. ESI HRMS m/z calcd for $\text{C}_{50}\text{H}_{62}\text{O}_2\text{Br}_4\text{Na}$ ($\text{M} + \text{Na}^+$) 1033.1381, found 1033.1382. Anal. Calcd for $\text{C}_{50}\text{H}_{62}\text{O}_2\text{Br}_4$: C, 59.19; H, 6.16. Found C, 58.97; H, 6.28.

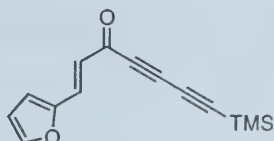
1,4-Bis[4-(4-*tert*-butylphenyl)-1,3-butadiynyl]-2,5-bis(octyloxy)benzene (215**).**



Dibromoolefin **213** (16 mg, 0.016 mmol) was reacted with *n*-BuLi (0.01 mL, 2.5 M in hexanes, 0.031 mmol) as per the general procedure to give tetrayne **215** (10.7 mg, 98%) as a yellow waxy solid: mp 118-119 °C; R_f = 0.8 (hexanes/EtOAc 9:1); IR

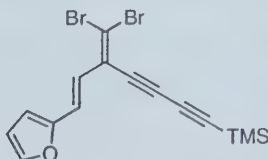
(CH₂Cl₂ cast) 2924, 2209, 2143, 1603, 1467, 1262, 1221 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 8.6 Hz, 4H), 7.34 (d, *J* = 8.6 Hz, 4H), 6.94 (s, 2H), 3.96 (t, *J* = 6.6 Hz, 4H), 1.80 (quint, *J* = 6.8 Hz, 4H), 1.47 (m, 4H), 1.30 (s, 18H), 1.27 (m, 16H), 0.85 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 154.8, 152.7, 132.3, 125.5, 118.8, 117.7, 113.6, 83.5, 79.7, 77.6, 73.6, 69.8, 34.9, 31.8, 31.1, 29.3, 29.26, 29.1, 26.0, 22.7, 14.1; EI HRMS *m/z* calcd for C₅₀H₆₂O₂ (M⁺) 694.4750, found 694.4742.

1-(2-Furyl)-7-trimethylsilylhept-1-en-4,6-diyn-3-one (218).



To a solution of 3-(2-furyl)acryloyl chloride (0.585 g, 3.73 mmol) in dry CH₂Cl₂ at 0 °C, 1,4-bis(trimethylsilyl)-1,3-butadiyne (0.726 g, 3.73 mmol) was added, followed by slow addition of AlCl₃ (0.498 g, 3.73 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/CH₂Cl₂, 2:1) gave the ketone **218** (0.535 g, 59%) as a reddish brown oil: *R*_f = 0.62 (CH₂Cl₂); IR (CH₂Cl₂ cast) 3127, 2962, 2209, 2098, 1621, 1593, 1550, 1469, 1266 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (m, 2H), 6.79 (d, *J* = 3.5 Hz, 1H), 6.66 (d, *J* = 15.8 Hz, 1H), 6.52 (ddd, *J* = 3.5, 1.8, 0.7 Hz, 1H), 0.24 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 176.1, 150.5, 146.1, 134.6, 125.8, 117.6, 113.0, 96.3, 86.0, 75.2, 72.2, -0.8; MS (EI, 70 eV) *m/z* 242.1 (M⁺, 72), 227.1 ([M - CH₃]⁺, 100); EI HRMS *m/z* calcd for C₁₄H₁₄O₂Si (M⁺) 242.0763, found 242.0766. Anal. Calcd for C₁₄H₁₄O₂Si: C, 69.38; H, 5.82. Found C, 69.01; H, 5.68.

[5-Dibromomethylene-7-(2-furyl)-hept-6-en-1,3-diynyl]trimethylsilane (219).



Ketone **218** (0.374 g, 1.54 mmol) was reacted with CBr₄ (1.033 g, 3.08 mmol) and PPh₃ (1.634 g, 6.17 mmol) as per the general procedure to give **219** (0.412 g, 67%) as

a yellow oil: $R_f = 0.33$ (hexanes); IR (CH_2Cl_2 cast) 2958, 2103, 1623, 1472, 1360, 1251 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.43 (d, $J = 1.8$ Hz, 1H), 6.90 (s, 2H), 6.48 (dd, $J = 3.4, 0.7$ Hz, 1H), 6.42 (d, $J = 3.4, 1.8$ Hz, 1H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 152.1, 143.4, 127.5, 123.2, 122.7, 112.1, 111.8, 102.1, 94.2, 87.1, 82.4, 71.5, -0.5 ; MS (EI, 70 eV) m/z 395.9/397.9/399.9 (M^+ , 22/43/21); HRMS m/z calcd for $\text{C}_{15}\text{H}_{14}\text{OSi}^{79}\text{Br}_2/\text{C}_{15}\text{H}_{14}\text{OSi}^{79}\text{Br}^{81}\text{Br}/\text{C}_{15}\text{H}_{14}\text{OSi}^{81}\text{Br}_2$ (M^+) 395.9181/397.9160/399.9140, found 395.9175/397.9157/399.9137.

[8-(2-Furyl)-oct-7-en-1,3,5-triynyl]trimethylsilane (**220**).



Dibromoolefin **219** (60.0 mg, 0.151 mmol) was reacted with *n*-BuLi (0.07 mL, 2.5 M in hexanes, 0.181 mmol) as per the general procedure to give triyne **220** (29.5 mg, 82%) as an orange oil: $R_f = 0.31$ (hexanes); IR (CHCl_3 cast) 2959, 2160, 2074, 2070, 1612, 1479, 1251 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.39 (d, $J = 1.6$ Hz, 1H), 6.87 (d, $J = 15.9$ Hz, 1H), 6.41 (m, 2H), 6.05 (d, $J = 15.9$ Hz, 1H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 151.6, 144.0, 132.8, 112.3, 112.0, 103.5, 89.6, 88.1, 77.3, 76.8, 67.9, 61.8, -0.5 ; EI HRMS m/z calcd for $\text{C}_{13}\text{H}_{14}\text{OSi}$ (M^+) 238.0814, found 238.0814.

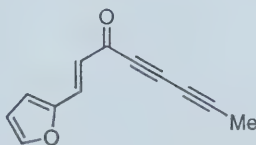
2-Non-1-en-3,5,7-triynylfuran (**216**) from **220**.*



To a solution of triyne **220** (0.132 g, 0.554 mmol) in a 1:1 mixture of methanol (5 mL) and THF (5 mL) at rt, K_2CO_3 (5 mg) was added. After the reaction mixture was stirred for 1 h, sat. aq. NH_4Cl (10 mL) was added and the solution was extracted with ether (20 mL). Evaporation of the solvent in vacuo yielded a white solid that was used directly in the next step. To a solution of the deprotected triyne in THF (10 mL) at -78°C , *n*-BuLi (0.22 mL, 2.5 M in hexanes, 0.55 mmol) was added. After the reaction mixture was stirred for 1 h, methyl iodide (0.70 mL, 1.6 g, 11 mmol) was added, the reaction was warmed to rt, quenched with sat. aq. NH_4Cl , and extracted

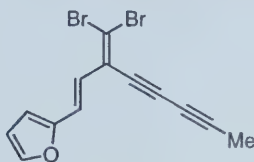
with ether. After removal of the solvent under reduced pressure, the resulting product was purified by flash column chromatography (SiO₂, hexanes) to give the triyne **216** (34.4 mg, 35%) as a white solid which darkens to a yellow color: mp 63–66 °C; R_f = 0.30 (hexanes); UV-Vis (THF) λ_{max} (ϵ) 272 (14600), 274 (14600), 287 (29100), 325 (19100), 340 (29900), 365 (29000) nm; IR (CH₂Cl₂ cast) 3119, 3013, 2913, 2219, 2199, 2166, 1612, 1479, 1261 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.38 (d, J = 1.3 Hz, 1H), 6.84 (d, J = 15.9 Hz, 1H), 6.40 (m, 2H), 6.04 (dd, J = 15.9, 0.4 Hz, 1H), 1.99 (s, 3H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 151.7, 143.8, 132.3, 112.2, 111.7, 103.9, 78.9, 77.7, 75.1, 68.5, 65.0, 59.2, 4.7; EI HRMS m/z calcd for C₁₃H₈O (M⁺) 180.0575, found 180.0574. *Spectral data were consistent with literature values: Bohlmann, F.; von Kap-Herr, W.; Fanghänel, L.; Arndt, C. *Chem. Ber.* **1965**, 98, 1411–1415.

1-(2-Furyl)-oct-1-en-4,6-diyn-3-one (**224**).



To a solution of 3-(2-furyl)acryloyl chloride (1.05 g, 6.71 mmol) in dry CH₂Cl₂ (25 mL) at 0 °C, trimethylsilylpenta-1,3-diyne (1.02 g, 7.46 mmol) was added, followed by slow addition of AlCl₃ (0.895 g, 6.71 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography gave the ketone **224** (0.694 g, 56%) as a bright yellow solid: mp 103–105 °C; R_f = 0.52 (CH₂Cl₂); IR (CH₂Cl₂ cast) 3119, 2234, 2189, 1607, 1561, 1462, 1310, 1279 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (m, 1H), 7.51 (d, J = 15.8 Hz, 1H), 6.77 (d, J = 3.5 Hz, 1H), 6.65 (d, J = 15.8 Hz, 1H), 6.51 (dd, J = 3.5, 1.8 Hz, 1H), 2.05 (s, 3H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 176.6, 150.5, 146.0, 134.3, 126.0, 117.3, 112.9, 85.4, 76.4, 70.5, 63.3, 4.8; EI HRMS m/z calcd for C₁₂H₈O₂ (M⁺) 184.0524, found 184.0523. Anal. Calcd for C₁₂H₈O₂: C, 78.25; H, 4.38. Found: C, 78.17; H, 4.31.

2-(3-Dibromomethylene-oct-1-en-4,6-diynyl)furan (225).



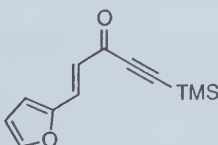
Ketone **224** (0.211 g, 1.14 mmol) was reacted with CBr₄ (0.759 g, 2.29 mmol) and PPh₃ (1.20 g, 4.58 mmol) as per the general procedure. Another equivalent of the brominating agent (0.759 g of CBr₄ and 1.20 g of PPh₃) was required for the reaction to reach completion, affording **225** (0.171 g, 44%) as an unstable white solid which turned rapidly yellow: mp 89-90 °C; *R_f* = 0.23 (hexanes); IR (CHCl₃ cast) 3057, 2911, 2851, 2239, 1621, 1511, 1474, 1384, 1269 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.42 (d, *J* = 1.8 Hz, 1H), 6.91 and 6.88 (AB quartet, *J* = 15.5 Hz, 2H), 6.45 (dd, *J* = 3.4, 0.6 Hz, 1H), 6.40 (dd, *J* = 3.4, 1.8 Hz, 1H), 2.01 (s, 3H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 152.2, 143.3, 127.8, 123.1, 122.9, 112.1, 111.7, 101.2, 83.7, 82.9, 69.1, 64.1, 4.8; MS (EI, 70 eV) *m/z* 337.9/339.9/341.9 (M⁺, 24/47/24); HRMS *m/z* calcd for C₁₃H₈O⁷⁹Br₂/C₁₃H₈O⁷⁹Br⁸¹Br/C₁₃H₈OSi⁸¹Br₂ (M⁺) 337.8942/339.8922/341.8901, found 337.8941/339.8922/341.8899.

2-Non-1-en-3,5,7-triynylfuran (216) from 222.



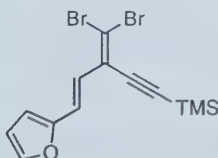
Dibromoolefin **222** (0.139 g, 0.407 mmol) was reacted with *n*-BuLi (0.20 mL, 2.5 M in hexanes, 0.49 mmol) as per the general procedure to give triyne **216** (61.9 mg, 84%) as a white solid which turns progressively yellow. Spectral data were consistent with that for the triyne **216** obtained from the previous procedure.

1-(2-Furyl)-5-trimethylsilylpent-1-en-4-yn-3-one (221).



To a solution of 3-(2-furyl)acryloyl chloride (2.98 g, 0.0190 mol) in dry CH_2Cl_2 at 0 °C, bis(trimethylsilyl)acetylene (3.24 g, 0.0190 mol) was added, followed by slow addition of AlCl_3 (2.54 g, 0.0190 mol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/ CH_2Cl_2 , 2:1) gave the ketone **221** (2.82 g, 68%) as a yellow oil which solidifies upon refrigeration to a yellow crystalline solid: mp 21-23 °C; R_f = 0.52 (CH_2Cl_2); IR (CH_2Cl_2 cast) 3126, 2961, 2925, 2854, 2155, 1652, 1623, 1552, 1470, 1251 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.53 (m, 1H), 7.526 (d, J = 15.8 Hz, 1H), 6.75 (d, J = 3.4 Hz, 1H), 6.64 (d, J = 15.8 Hz, 1H), 6.51 (m, 1H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 177.3, 150.6, 145.8, 134.1, 125.7, 117.0, 112.9, 100.6, 98.2, -0.7; MS (EI, 70 eV) m/z 218.1 (M^+ , 57), 203.1 ($[\text{M} - \text{CH}_3]^+$, 100); EI HRMS m/z calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{Si}$ (M^+) 218.0763, found 218.0764. Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{Si}$: C, 66.01; H, 6.46. Found: C, 65.61; H, 6.54.

[3-Dibromomethylene-5-(2-furyl)-pent-4-en-1-ynyl]trimethylsilane (**222**).



Ketone **221** (0.159 g, 0.728 mmol) was reacted with CBr_4 (0.488 g, 1.46 mmol) and PPh_3 (0.772 g, 2.91 mmol) as per the general procedure to give **222** (0.157 g, 58%) as a pale yellow oil which should be kept refrigerated (rapid decomposition occurs at rt): R_f = 0.33 (hexanes); IR (CH_2Cl_2 cast) 2959, 2145, 1621, 1476, 1251 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.43 (d, J = 1.7 Hz, 1H), 6.93 and 6.91 (AB quartet, J = 15.5 Hz, 2H), 6.46 (d, J = 3.3 Hz, 1H), 6.42 (dd, J = 3.3, 1.7 Hz, 1H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 152.4, 143.2, 128.6, 123.2, 123.0, 112.0, 111.3, 104.7, 100.3, 99.5, -0.3; MS (EI, 70 eV) m/z 371.9/373.9/375.9 (M^+ , 25/58/29); HRMS m/z calcd for $\text{C}_{13}\text{H}_{14}\text{O}\text{Si}^{79}\text{Br}_2/\text{C}_{13}\text{H}_{14}\text{OSi}^{79}\text{Br}^{81}\text{Br}/\text{C}_{13}\text{H}_{14}\text{OSi}^{81}\text{Br}_2$ (M^+) 371.9181/373.9160/375.9140, found 371.9172/373.9157/375.9154.

[6-(2-Furyl)-hex-5-ene-1,3-diynyl]trimethylsilane (223).



Dibromoolefin **222** (0.912 g, 2.44 mmol) was reacted with *n*-BuLi (1.17 mL, 2.5 M in hexanes, 2.92 mmol) as per the general procedure to give diyne **223** (0.366 g, 70%) as a yellow oil: R_f = 0.3 (hexanes); IR (CHCl₃ cast) 2959, 2925, 2188, 2101, 1616, 1479, 1251 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.37 (d, J = 1.8 Hz, 1H), 6.80 (d, J = 16.0 Hz, 1H), 6.41 (dd, J = 3.4, 1.8 Hz, 1H), 6.37 (d, J = 3.4 Hz, 1H), 6.04 (d, J = 16.0 Hz, 1H), 0.20 (s, 9H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 151.7, 143.6, 131.6, 112.1, 111.4, 104.2, 91.7, 88.0, 77.1, 76.5, -0.4; EI HRMS m/z calcd for C₁₃H₁₄OSi (M⁺) 214.0814, found 214.0814.

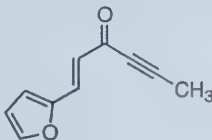
2-Hept-1-ene-3,5-diynylfuran (217) from 223.



To a solution of diyne **223** (0.108 g, 0.505 mmol) in a 1:1 mixture of methanol (5 mL) and THF (5 mL) at rt, K₂CO₃ (0.2 equiv.) was added. After the reaction mixture was stirred for one hour, sat. aq. NH₄Cl (10 mL) was added and the solution mixture was then extracted with ether. Evaporation of the solvent *in vacuo* yielded a white solid that was used directly in the next step. To a solution of the deprotected diyne in THF at -78 °C, *n*-BuLi (0.2 mL, 2.5 M in hexanes, 0.505 mmol) was added. After the reaction mixture was stirred for 1 h, methyl iodide (0.64 mL, 1.45 g, 10.1 mmol) was added, and the reaction mixture was stirred and allowed to warm to rt. The reaction mixture was quenched with sat. aq. NH₄Cl and extracted with ether. After removal of the solvent under reduced pressure, the resulting product was purified by flash column chromatography (SiO₂, hexanes) to give the diyne **217** (31.2 mg, 40%) as a yellow oil: R_f = 0.25 (hexanes); IR (CHCl₃ cast) 3117, 3046, 2912, 2841, 2230, 2138, 1618, 1480, 1262 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, J = 1.8 Hz, 1H), 6.77 (d, J = 16.0 Hz, 1H), 6.40 (dd, J = 3.4, 1.8 Hz, 1H), 6.34 (d, J = 3.4 Hz, 1H), 6.04 (d, J = 16.0 Hz, 1H), 1.99 (s, 3H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 151.9, 143.3, 130.7, 112.0,

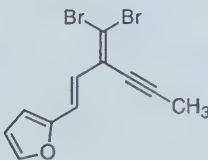
110.7, 105.0, 81.3, 77.4, 73.8, 64.6, 4.7; EI HRMS m/z calcd for $C_{11}H_8O$ (M^+) 156.0575, found 156.0575.

1-(2-Furyl)-hex-1-en-4-yn-3-one (226).



To a solution of 3-(2-furyl)acryloyl chloride (0.842 g, 5.38 mmol) in dry CH_2Cl_2 at 0 °C, trimethylsilylpropyne (0.604 g, 5.38 mmol) was added, followed by slow addition of $AlCl_3$ (0.717 g, 5.38 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/ CH_2Cl_2 , 4:1) gave the ketone **226** (0.596 g, 69%) as an orange oil: R_f = 0.46 (CH_2Cl_2); IR (CH_2Cl_2 cast) 3125, 2223, 1617, 1551, 1470, 1263 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 15.8 Hz, 1H), 7.517 (m, 1H), 6.73 (d, J = 3.5 Hz, 1H), 6.61 (d, J = 15.8 Hz, 1H), 6.50 (dd, J = 3.5, 1.8 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, APT, $CDCl_3$) δ 177.9, 150.6, 145.6, 133.7, 126.1, 116.6, 112.8, 90.3, 78.5, 4.1; EI HRMS m/z calcd for $C_{10}H_8O_2$ (M^+) 160.0524, found 160.0523.

2-(3-Dibromomethylene-hex-1-en-4-ynyl)furan (227).



Ketone **226** (0.463 g, 2.89 mmol) was reacted with CBr_4 (1.92 g, 5.78 mmol) and PPh_3 (3.30 g, 11.6 mmol) as per the general procedure to give **227** (0.281 g, 31%) as an unstable orange oil which should be kept refrigerated: R_f = 0.30 (hexanes); IR (CH_2Cl_2 cast) 3114, 2915, 2850, 2230, 1621, 1475, 1268 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 1.8 Hz, 1H), 6.95 and 6.90 (AB quartet, J = 15.4 Hz, 2H), 6.44 (d, J = 3.3 Hz, 1H), 6.41 (dd, J = 3.3, 1.8 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, APT, $CDCl_3$) δ 152.5, 143.1, 128.8, 123.5, 122.9, 112.0, 111.0, 98.2, 95.6, 75.4, 4.7; MS (EI, 70 eV) m/z 313.9/315.9/317.9 (M^+ , 12/23/12); HRMS m/z calcd for

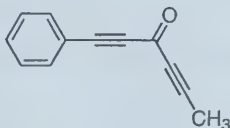
$\text{C}_{11}\text{H}_8\text{O}^{79}\text{Br}_2/\text{C}_{11}\text{H}_8\text{O}^{79}\text{Br}^{81}\text{Br}/\text{C}_{11}\text{H}_8\text{OSi}^{81}\text{Br}_2$ (M^+) 313.8942/315.8922/317.8901, found 313.8939/315.8920/317.8907.

2-Hept-1-ene-3,5-diynylfuran (**217**) from **227**.



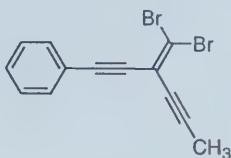
Dibromoolefin **227** (0.129 g, 0.409 mmol) was reacted with *n*-BuLi (0.20 mL, 2.5 M in hexanes, 0.491 mmol) as per the general procedure to give diyne **217** (37.4 mg, 59%) as a yellow oil. Spectral data were consistent with that for the diyne **217** obtained from the previous procedure.

1-Phenyl-hexa-1,4-diyn-3-one (**228**).*



To a solution of phenylpropiolyl chloride (0.885 g, 5.38 mmol) in dry CH_2Cl_2 at 0°C , trimethylsilylpropyne (0.604 g, 5.38 mmol) was added, followed by slow addition of AlCl_3 (0.717 g, 5.38 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/ CH_2Cl_2 , 5:1) gave the ketone **228** (0.504 g, 56%) as a yellow solid: mp $66\text{--}68^\circ\text{C}$; $R_f = 0.82$ (CH_2Cl_2); IR (CH_2Cl_2 cast) 2227, 2197, 1620, 1490, 1444 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.60 (m, 2H), 7.45 (m, 1H), 7.38 (m, 2H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 161.0, 133.2, 131.0, 128.6, 119.5, 91.5, 90.5, 89.2, 81.5, 4.4; EI HRMS m/z calcd for $\text{C}_{12}\text{H}_8\text{O}$ (M^+) 168.0575, found 168.0578. *Spectral data consistent with published results: Rule, G. N.; Detty, M. R.; Kaeding, J. E.; Sinicropi, J. A. *J. Org. Chem.* **1995**, 60, 1665-1673.

(3-Dibromomethylene-hexa-1,4-diynyl)benzene (**229**).



Ketone **228** (0.102 g, 0.608 mmol) was reacted with CBr_4 (0.403 g, 1.22 mmol) and PPh_3 (0.638 g, 2.43 mmol) as per the general procedure to give **229** (0.131 g, 67%) as a pale yellow oil: $R_f = 0.35$ (hexanes); IR (CH_2Cl_2 cast) 3054, 2915, 2849, 2242, 2215, 1597, 1571, 1487, 1442 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.44 (m, 2H), 7.33 (m, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 131.6, 129.1, 128.4, 122.2, 114.4, 106.4, 95.1, 93.8, 86.4, 76.7, 4.8; MS (EI, 70 eV) m/z 321.9/323.9/325.9 (M^+ , 51/100/50); HRMS m/z calcd for $\text{C}_{13}\text{H}_8^{79}\text{Br}_2/\text{C}_{13}\text{H}_8^{79}\text{Br}^{81}\text{Br}/\text{C}_{13}\text{H}_8^{81}\text{Br}_2$ (M^+) 321.8993/323.8972/325.8952, found 321.8999/323.8975/325.8956. Anal. Calcd for $\text{C}_{13}\text{H}_8\text{Br}_2$: C, 48.19; H, 2.49. Found: C, 48.00; H, 2.35.

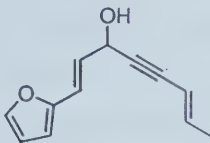
1-Phenylhepta-1,3,5-triyne (**167**).*



Dibromoolefin **229** (0.131 g, 0.404 mmol) was reacted with *n*-BuLi (0.19 mL, 2.5 M in hexanes, 0.485 mmol) as per the general procedure to give triyne **167** (31.9 mg, 48%) as a white solid: mp 58°C; $R_f = 0.40$ (hexanes); UV-Vis (THF) λ_{max} (ϵ) 241 (61600), 252 (172000), 276 (10100), 292 (19600), 311 (26700), 333 (19700) nm; IR (CH_2Cl_2 cast) 2220, 1593, 1490, 1441 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.49 (m, 2H), 7.32 (m, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 132.9, 129.4, 128.4, 121.1, 78.2, 75.2, 74.6, 67.4, 64.9, 58.9, 4.6; EI HRMS m/z calcd. for C_{13}H_8 (M^+) 164.0626, found 164.0624. Anal. Calcd for C_{13}H_8 : C, 95.09; H, 4.91. Found C, 94.69; H, 4.64. *Spectral data were consistent with literature values: (a) Alvarez, L.; Marquina, S.; Villarreal, M. L.; Alonso, D.; Aranda, E.; Delgado, G. *Planta Med.* **1996**, 62, 355–357. (b) Kawazu, K.; Nishii, Y.; Nakajima, S. *Agric. Biol. Chem.* **1980**, 44, 903–906. (c) Shim, S. C.; Lee, T. S. *Chem. Lett.* **1986**, 1075–1078. (d)

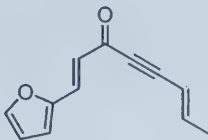
Chang, M. H.; Wang, G. J.; Kuo, Y. H.; Lee, C. K. *J. Chin. Chem. Soc.* **2000**, *47*, 1131–1136.

1-(2-Furyl)-octa-1,6-dien-4-yn-3-ol (231).



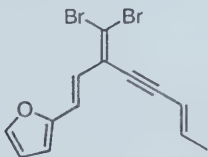
Crotonaldehyde (0.505 g, 7.13 mmol) was reacted with CBr_4 (4.73 g, 14.3 mmol) and PPh_3 (7.48 g, 28.5 mmol) as per the general procedure to give 1,1-dibromo(1*E*,3*E*)-1,3-pentadiene (1.401 g, 87%).* To a solution of this dibromoolefin (1.401 g, 6.20 mmol) in THF at -78°C was added *n*-BuLi (5.21 mL, 2.5 M in hexanes, 13.0 mmol). After the reaction mixture was stirred for 1 h at -78°C and for a further hour at rt, furanacrolein (0.682 g, 5.58 mmol) in THF (5 mL) was added at -78°C . The reaction mixture was slowly warmed to rt until the reaction was judged complete by TLC analysis. The reaction was quenched with satd. aq. NH_4Cl at -78°C , and the solution mixture was extracted with ether. Evaporation of the solvent, and purification by column chromatography (CH_2Cl_2 /hexanes, 3:4) yielded alcohol **231** (0.568 g, 54%) as an orange oil; R_f = 0.30 (CH_2Cl_2); IR (CH_2Cl_2 cast) 3351, 3027, 2914, 2101, 1629, 1488, 1443, 1384, 1296, 1258 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.34 (d, J = 1.8 Hz, 1H), 6.57 (dd, J = 15.7, 1.4 Hz, 1H), 6.35 (dd, J = 3.3, 1.8 Hz, 1H), 6.28 (d, J = 3.3 Hz, 1H), 6.23 (dd, J = 15.7, 5.8 Hz, 1H), 6.19 (ddq, J = 15.8, 6.8, 0.5 Hz, 1H), 5.53 (app. dq, J = 15.8, 1.8 Hz, 1H), 5.10 (bs, 1H), 2.01 (bs, 1H), 1.77 (ddd, J = 6.8, 1.8, 0.5 Hz, 3H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 151.8, 142.4, 140.7, 126.7, 119.8, 111.3, 109.9, 109.1, 85.8, 85.2, 63.0, 18.6; EI HRMS m/z calcd for $\text{C}_{12}\text{H}_{12}\text{O}_2$ (M^+) 188.0837, found 188.0836. *Previously reported by: Bestmann, H. J.; Frey, H. *Liebigs Ann. Chem.* **1980**, 2061–2071.

1-(2-Furyl)-octa-1,6-dien-4-yn-3-one (232).



To the alcohol **231** (0.181 g, 0.961 mmol) in CH_2Cl_2 was added manganese dioxide (1.00 g, 11.53 mmol, 12 equiv). After the reaction mixture was stirred at rt until the reaction was judged complete by TLC analysis, the solution mixture was filtered through a pad of Celite. After removal of the solvent under reduced pressure, the resulting crude product was recrystallized from methanol–water to give ketone **232** (0.105 g, 59%) as colorless needle-like crystals: mp 53–55 °C; R_f = 0.31 (CH_2Cl_2); IR (CHCl_3 cast) 3124, 3031, 2914, 2191, 1616, 1551 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.53 (d, J = 1.8 Hz, 1H), 7.50 (d, J = 15.7 Hz, 1H), 6.73 (d, J = 3.4 Hz, 1H), 6.66 (d, J = 15.7 Hz, 1H), 6.54 (dq, J = 15.8, 6.9 Hz, 1H), 6.50 (dd, J = 3.4, 1.8 Hz, 1H), 5.69 (dq, J = 15.8, 1.8 Hz, 1H), 1.89 (dd, J = 6.9, 1.8 Hz, 3H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 177.8, 150.7, 147.0, 145.7, 133.4, 126.2, 116.6, 112.8, 109.0, 90.6, 85.6, 19.2; MS (EI, 70 eV) m/z 186.1 (M^+ , 76), 171.0 ($[\text{M} - \text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{12}\text{H}_{10}\text{O}_2$ (M^+) 186.0681, found 186.0675. Anal. Calcd for $\text{C}_{12}\text{H}_{10}\text{O}_2$: C, 77.40; H, 5.41. Found C, 77.59; H, 5.32

2-(3-Dibromomethylene-octa-1,6-dien-4-ynyl)furan (233).



Ketone **232** (0.057 g, 0.31 mmol) was reacted with CBr_4 (0.203 g, 0.611 mmol) and PPh_3 (0.321 g, 1.22 mmol) as per the general procedure to give **233** (60.9 mg, 58%) as a relatively unstable pale yellow oil; R_f = 0.24 (hexanes); IR (CHCl_3 cast) 3027, 2923, 2851, 2201, 1624, 1510, 1474, 1441 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.42 (d, J = 1.8 Hz, 1H), 6.95 and 6.88 (AB quartet, J = 15.4 Hz, 2H), 6.43 (d, J = 3.4 Hz, 1H), 6.40 (dd, J = 3.4, 1.8 Hz, 1H), 6.34 (dq, J = 15.8, 6.9 Hz, 1H), 5.71 (dq, J = 15.8, 1.8 Hz, 1H), 1.84 (dd, J = 6.9, 1.8 Hz, 3H); ^{13}C NMR (100 MHz, APT, CDCl_3) δ 152.4,

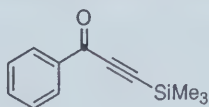
143.2, 141.7, 128.7, 123.2, 123.0, 112.0, 111.2, 110.3, 98.6, 97.2, 83.1, 18.9; MS (EI, 70 eV) m/z 339.9/341.9/343.9 (M^+ , 9/17/8), 182.1 ($[M - Br_2]^+$, 100); HRMS m/z calcd for $C_{13}H_{10}O^{79}Br_2/C_{13}H_{10}O^{79}Br^{81}Br/C_{13}H_{10}O^{81}Br_2$ (M^+) 339.9099/341.9078/343.9057, found 339.9094/341.9076/343.9057.

Atractylodin (12).*



Dibromoolefin **233** (0.145 g, 0.424 mmol) was reacted with *n*-BuLi (0.20 mL, 2.5 M in hexanes, 0.51 mmol) as per the general procedure and purified by column chromatography (pentane) to give diyne **12** (55.9 mg, 72%) as a white solid which turns progressively pale yellow: mp 50–52 °C; R_f = 0.18 (hexanes); UV-Vis (THF) λ_{max} (ϵ) 260 (11500), 273 (12600), 339 (32700) nm; IR (CDCl₃ cast) 3113, 2182, 2124, 1616, 1477, 1442 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.37 (m, 1H), 6.77 (d, J = 15.9 Hz, 1H), 6.40 (dd, J = 3.4, 1.8 Hz, 1H), 6.35 (m, 1H), 6.31 (m, 1H), 6.09 (d, J = 15.9 Hz, 1H), 5.58 (m, 1H), 1.82 (dd, J = 6.9, 1.8 Hz, 3H); ¹³C NMR (100 MHz, APT, CDCl₃) δ 151.9, 143.6, 143.5, 130.7, 112.1, 111.0, 110.0, 104.9, 81.9, 80.2, 77.2, 72.5, 18.9; EI HRMS m/z calcd for $C_{13}H_{10}O$ (M^+) 182.0732, found 182.0732. *¹H and ¹³C NMR spectral data were consistent with literature values: (a) Yosioka, I.; Hikino, H.; Sasaki, Y. *Chem. Pharm. Bull.* **1960**, 8, 957–959. (b) Nishikawa, Y.; Yasuda, I.; Watanabe, Y.; Seto, T. *Yakugaku Zasshi* **1976**, 96, 1322–1326.

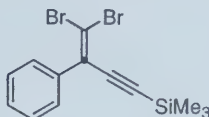
1-¹³C-1-Phenyl-3-trimethylsilylpropynone (242).



To benzoic-carboxy-¹³C acid (**240**) (0.201 g, 1.63 mmol) was added thionyl chloride (6 mL). The reaction mixture was heated under reflux for an hour and the excess thionyl chloride was evaporated under vacuo to yield acid chloride **241**, which was used directly in the next step. To a solution of **241** in dry CH₂Cl₂ (8 mL) at 0 °C, (triisopropylsilyl)trimethylsilylacetylene (0.278 g, 1.63 mmol) was added, followed by

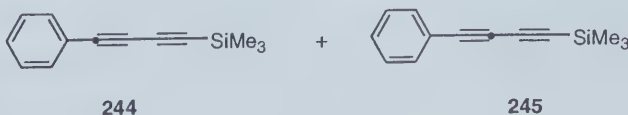
slow addition of AlCl_3 (0.217 g, 1.63 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/ CH_2Cl_2 , 10:1) gave the ketone **242** (0.208 g, 63%) as a colorless oil: R_f = 0.73 (CHCl_3); IR (CHCl_3 cast) 3066, 2960, 2152, 1611, 1596, 1576, 1450 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.13 (m, 2H), 7.45 (m, 1H), 7.60 (dd, J = 7.4 Hz, 1H), 7.47 (dd, J = 7.9 Hz, 2H), 0.30 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.7, 136.5 (d, J = 61 Hz), 134.2, 129.6 (d, J = 4 Hz), 128.6 (d, J = 6 Hz), 100.8 (d, J = 86 Hz), 100.5 (d, J = 10 Hz), -0.7; MS (EI, 70 eV) m/z 203.1 (M^+ , 33), 188.1 ($[\text{M} - \text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{11}^{13}\text{CH}_{14}\text{OSi}$ (M^+) 203.0848, found 203.0840.

(4,4-Dibromo-3- ^{13}C -3-phenylbuten-1-ynyl)trimethylsilane (243**).**



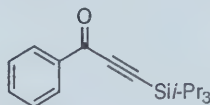
Ketone **242** (0.153 g, 0.753 mmol) was reacted with CBr_4 (0.542 g, 1.51 mmol) and PPh_3 (0.798 g, 3.01 mmol) in CH_2Cl_2 as per the general procedure. Another equivalent of the brominating agent (0.542 g CBr_4 and 0.798 g PPh_3) was added after 1 h to force the reaction to completion to give **243** (0.266 g, 98%) as a pale yellow oil: R_f = 0.43 (hexanes); IR (CHCl_3 cast) 3045, 2958, 2155, 1506, 1442 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.41 (m, 2H), 7.35 (m, 3H), 0.20 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.8 (d, J = 58 Hz), 130.9, 128.5 (d, J = 2 Hz), 128.48 (d, J = 1 Hz), 128.3 (d, J = 4 Hz), 104.1 (d, J = 8 Hz), 103.3 (d, J = 88 Hz), 100.2 (d, J = 90 Hz), -0.4; MS (EI, 70 eV) m/z 356.9/358.9/360.9 (M^+ , 48/100/52); HRMS m/z calcd for $\text{C}_{12}^{13}\text{CH}_{14}\text{Si}^{79}\text{Br}_2/\text{C}_{12}^{13}\text{CH}_{14}\text{Si}^{79}\text{Br}^{81}\text{Br}/\text{C}_{12}^{13}\text{CH}_{14}\text{Si}^{81}\text{Br}_2$ (M^+) 356.9265/358.9245/360.9224, found 356.9264/358.9243/360.9223.

(4- ^{13}C -4-Phenyl)-1,3-butadiynyl)trimethylsilane (244**) and (3- ^{13}C -4-phenyl)-1,3-butadiynyl)trimethylsilane (**245**).**



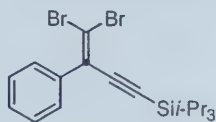
Dibromoolefin **243** (0.240 g, 0.668 mmol) was reacted with *n*-BuLi (0.32 mL, 2.5 M in hexanes, 0.80 mmol) as per the general procedure and purified by column chromatography (hexanes) to give an inseparable 45:55 mixture of diynes **244** and **245** (0.132 g, 99%) as a yellow oil: R_f = 0.48 (hexanes); IR (CHCl₃ cast) 3085, 2959, 2924, 2175, 2096, 1489, 1442 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.47 (m, 2H), 7.32 (m, 3H), 0.22 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 132.6 (d, J = 3 Hz) and (d, J = 2 Hz), 129.3 (d, J = 1 Hz), 128.4 (s) and (d, J = 6 Hz), 121.4 (d, J = 92 Hz) and (d, J = 14 Hz), 90.6 (d, J = 14 Hz), 87.8 (d, J = 148 Hz) and (d, J = 18 Hz), 76.1, 76.1 and 74.1 (AB quartet, J = 196 Hz), 74.1, -0.4; **244**: ¹³C NMR (100 MHz, CDCl₃) δ 132.6 (d, J = 3 Hz), 129.3 (d, J = 1 Hz), 128.4 (d, J = 6 Hz), 121.4 (d, J = 92 Hz), 90.6 (d, J = 14 Hz), 87.8 (d, J = 18 Hz), 76.1, 74.1 (Half of AB quartet, J = 196 Hz), -0.4; **245**: ¹³C NMR (100 MHz, CDCl₃) δ 132.6 (d, J = 2 Hz), 129.3, 128.4 (s), 121.4 (d, J = 14 Hz), 90.6 (d, J = 14 Hz), 87.8 (d, J = 148 Hz), 76.1, 76.1 (Half of AB quartet, J = 196 Hz), 74.1, -0.4; MS (EI, 70 eV) m/z 199.1 (M⁺, 29), 184.1 ([M - CH₃]⁺, 100); HRMS m/z calcd for C₁₂¹³CH₁₄Si (M⁺) 199.0898, found 199.0900.

1-¹³C-1-Phenyl-3-triisopropylsilylpropynone (**246**).



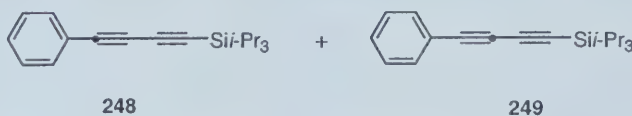
To a solution of acid chloride **241** (0.170 g, 1.21 mmol) in dry CH₂Cl₂ (6 mL) at 0 °C, (triisopropylsilyl)trimethylsilylacetylene (0.305 g, 1.20 mmol) was added, followed by slow addition of AlCl₃ (0.161 g, 1.22 mmol). The reaction mixture was stirred for 3 h. Aqueous work-up and purification by column chromatography (hexanes/CH₂Cl₂, 10:1) gave the ketone **246** (0.254 g, 73%) as a colorless oil: R_f = 0.82 (CH₂Cl₂); IR (CHCl₃ cast) 3066, 2944, 2892, 2866, 2147, 1611, 1597, 1576, 1463, 1449 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.16 (m, 2H), 7.59 (m, 1H), 7.47 (m, 2H), 1.15 (m, 21H); ¹³C NMR (100 MHz, CDCl₃) δ 177.4, 136.7 (d, J = 61 Hz), 134.0 (d, J = 1 Hz), 129.5 (d, J = 3 Hz), 128.5 (d, J = 5 Hz), 103.0 (d, J = 84 Hz), 97.9 (d, J = 9 Hz), 18.5, 11.1; MS (EI, 70 eV) m/z 287.2 (M⁺, 63), 244.1 ([M - C₃H₇]⁺, 100); HRMS m/z calcd for C₁₇¹³CH₂₆OSi (M⁺) 287.1787, found 287.1791.

(4,4-Dibromo-3-¹³C-3-phenylbuten-1-ynyl)triisopropylsilane (247).



Ketone **246** (0.184 g, 0.640 mmol) was reacted with CBr₄ (0.426 g, 1.30 mmol) and PPh₃ (0.665 g, 2.54 mmol) as per the general procedure to give **247** (0.250 g, 89%) as a colorless oil: *R_f* = 0.91 (CH₂Cl₂); IR (CHCl₃ cast) 3059, 3022, 2942, 2890, 2864, 2153, 1505, 1463, 1442 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.47 (m, 2H), 7.35 (m, 3H), 0.20 (s, 21H); ¹³C NMR (100 MHz, CDCl₃) δ 138.0 (d, *J* = 58 Hz), 131.2, 128.6 (d, *J* = 2 Hz), 128.4, 128.2 (d, *J* = 4 Hz), 105.2 (d, *J* = 88 Hz), 101.2 (d, *J* = 8 Hz), 99.5 (d, *J* = 90 Hz), 18.6, 11.2; MS (EI, 70 eV) *m/z* 441.0/443.0/445.0 (M⁺, 12/28/15); HRMS *m/z* calcd for C₁₈¹³CH₂₆Si⁷⁹Br₂/C₁₈¹³CH₂₆Si⁷⁹Br⁸¹Br/C₁₈¹³CH₂₆Si⁸¹Br₂ (M⁺) 441.0204/443.0184/445.0164, found 441.0191/443.0157/445.0108.

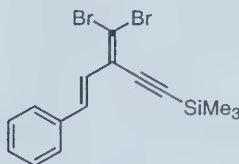
(4-¹³C-4-Phenyl)-1,3-butadiynyl)triisopropylsilane (248) and (3-¹³C-4-phenyl)-1,3-butadiynyl)triisopropylsilane (249).



Dibromoolefin **247** (0.205 g, 0.465 mmol) was reacted with *n*-BuLi (0.22 mL, 2.5 M in hexanes, 0.55 mmol) as per the general procedure and purified by column chromatography (pentane) to give an inseparable 1:2 mixture of diynes **248** and **249** (0.121 g, 92%) as a colorless oil: *R_f* = 0.55 (hexanes); IR (CH₂Cl₂ cast) 3061, 2943, 2890, 2865, 2173, 2094, 1595, 1488, 1462, 1442 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.49 (m, 2H), 7.30 (m, 3H), 1.10 (s, 21H); ¹³C NMR (100 MHz, CDCl₃) δ 132.6 (d, *J* = 3 Hz) and (d, *J* = 2 Hz), 129.2 (d, *J* = 1 Hz), 128.3 (s) and (d, *J* = 6 Hz), 121.5 (d, *J* = 95 Hz) and (d, *J* = 14 Hz), 89.5 (d, *J* = 147 Hz) and (d, *J* = 17 Hz), 87.8 (d, *J* = 14 Hz), 75.5, 75.5 and 74.6 (AB quartet, *J* = 207 Hz), 74.6, 18.6, 11.3; **248**: ¹³C NMR (100 MHz, CDCl₃) δ 132.6 (d, *J* = 3 Hz), 129.2 (d, *J* = 1 Hz), 128.3 (d, *J* = 6 Hz), 121.5 (d, *J* = 95 Hz), 89.5 (d, *J* = 17 Hz), 87.8 (d, *J* = 14 Hz), 75.5, 74.6 (Half of AB

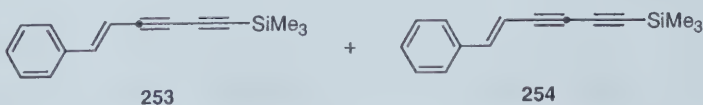
quartet, $J = 207$ Hz), 18.6, 11.3; **249**: ^{13}C NMR (100 MHz, CDCl_3) δ 132.6 (d, $J = 2$ Hz), 129.2, 128.3 (s), 121.5 (d, $J = 14$ Hz), 89.5 (d, $J = 147$ Hz), 87.8 (d, $J = 14$ Hz), 75.5 (Half of AB quartet, $J = 207$ Hz), 74.6, 18.6, 11.3; MS (EI, 70 eV) m/z 283.2 (M^+ , 25), 240.1 ($[\text{M} - \text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{18}^{13}\text{CH}_{26}\text{Si}$ (M^+) 283.1838, found 283.1833.

(3- ^{13}C -3-Dibromomethylene-5-phenylpent-4-en-1-ynyl)trimethylsilane (252).



Ketone **199I** (0.115 g, 0.503 mmol) was reacted with $^{13}\text{CBr}_4$ (0.206 g, 0.621 mmol) and PPh_3 (0.329 g, 1.24 mmol) as per the general procedure to give **252** (0.124 g, 64%) as a colorless oil: $R_f = 0.48$ (hexanes); IR (CH_2Cl_2 cast) 3025, 2958, 2924, 2145, 1616, 1488, 1447 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.47 (m, 2H), 7.33 (m, 3H), 7.16 (dd, $J = 15.6, 1.7$ Hz, 1H), 7.01 (dd, $J_{\text{HH}} = 15.6, J_{\text{CH}} 4.8$ Hz, 1H), 0.29 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 136.4, 136.3, 128.8 (d, $J = 90$ Hz), 128.8, 128.6, 127.2 (d, $J = 2$ Hz), 124.7, 104.9 (d, $J = 5$ Hz), 100.6, 99.8 (d, $J = 2$ Hz), -0.3 ; MS (EI, 70 eV) m/z 382.9/384.9/386.9 (M^+ , 14/28/15), 225.1 ($[\text{M}-\text{Br}_2]^+$, 100); HRMS m/z calcd for $\text{C}_{14}^{13}\text{CH}_{16}\text{Si}^{79}\text{Br}_2/\text{C}_{14}^{13}\text{CH}_{16}\text{Si}^{79}\text{Br}^{81}\text{Br}/\text{C}_{14}^{13}\text{CH}_{16}\text{Si}^{81}\text{Br}_2$ (M^+) 382.9422/384.9401/386.9381, found 382.9416/384.9399/386.9381.

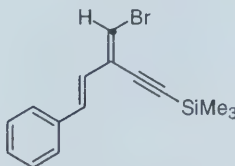
(4- ^{13}C -6-Phenyl-hex-5-ene-1,3-diynyl)trimethylsilane (253) and (3- ^{13}C -6-phenyl-hex-5-ene-1,3-diynyl)trimethylsilane (254).



Dibromoolefin **252** (124 mg, 0.321 mmol) was reacted with $n\text{-BuLi}$ (0.30 mL, 2.5 M in hexanes, 0.77 mmol) as per the general procedure and purified by column chromatography (pentane) to give an inseparable 57:43 mixture of diynes **253** and **254** (60.5 mg, 84%) as a colorless oil: $R_f = 0.32$ (hexanes); IR (CHCl_3 cast) 3030, 2959,

2161, 2084, 1604, 1491, 1448 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.34 (m, 5H), 7.08 (d, $J = 16.2$ Hz, 1H), 6.15 (dd, $J_{\text{HH}} = 16.2$, $J_{\text{HC}} = 2.4$ Hz, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.1 (d, $J = 5$ Hz) and (d, $J = 1$ Hz), 135.6 (s) and (d, $J = 9$ Hz), 129.3, 128.8, 126.4, 106.3 (d, $J = 13$ Hz) and (d, $J = 93$ Hz), 91.3 (d, $J = 14$ Hz), 88.0 (d, $J = 148$ Hz) and (d, $J = 18$ Hz), 76.5, 76.5 and 76.3 (AB quartet, $J = 170$ Hz), 76.3, -0.4 ; **253**: ^{13}C NMR (100 MHz, CDCl_3) δ 145.1 (d, $J = 1$ Hz), 135.6 (d, $J = 9$ Hz), 129.3, 128.8, 126.4, 106.3 (d, $J = 93$ Hz), 91.3 (d, $J = 14$ Hz), 88.0 (d, $J = 18$ Hz), 76.5, 76.3 (Half of AB quartet, $J = 170$ Hz), -0.4 ; **254**: ^{13}C NMR (100 MHz, CDCl_3) δ 145.1 (d, $J = 5$ Hz), 135.6 (s), 129.3, 128.8, 126.4, 106.3 (d, $J = 13$ Hz), 91.3 (d, $J = 14$ Hz), 88.0 (d, $J = 148$ Hz), 76.5 (Half of AB quartet, $J = 170$ Hz), 76.3, -0.4 ; MS (EI, 70 eV) m/z 225.1 (M^+ , 39), 210.1 ($[\text{M} - \text{CH}_3]^+$, 100); HRMS m/z calcd for $\text{C}_{14}^{13}\text{CH}_{16}\text{Si}$ (M^+) 225.1055, found 225.1055.

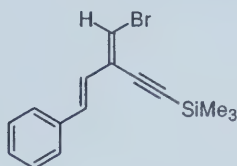
[3-(Bromo- ^{13}C -methylene)-5-phenylpent-4-en-1-ynyl]trimethylsilane (255).*



Compound **255** was obtained as a white solid: $R_f = 0.2$ (hexanes); IR (CH_2Cl_2 cast) 3069, 2960, 2924, 2852, 2148, 1446 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.42 (m, 2H), 7.32 (m, 2H), 7.27 (m, 1H), 7.03 (d, $J = 15.6$ Hz, 1H), 6.71 (d, $J = 196$ Hz, 1H), 6.66 (dd, $J = 15.6$, 5.4 Hz, 1H), 0.30 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 136.4 (d, $J = 1$ Hz), 132.9 (d, $J = 9$ Hz), 129.6 (d, $J = 81$ Hz), 128.7, 128.1, 126.8, 125.7 (d, $J = 5$ Hz), 115.8, 104.7 (d, $J = 4$ Hz), 98.8 (d, $J = 3$ Hz), -0.2 ; GOESY (500 MHz, CDCl_3): Irradiation at δ 6.67 results in enhancement of signals at δ 6.72, 7.04, 7.43; MS (EI, 70 eV) m/z 305.0/307.0 (M^+ , 8/8); HRMS m/z calcd for $\text{C}_{14}^{13}\text{CH}_{17}\text{Si}^{79}\text{Br}/\text{C}_{14}^{13}\text{CH}_{17}\text{Si}^{81}\text{Br}$ (M^+) 305.0317/307.0296, found 305.0318/307.0297.

*GOESY spectrum is shown in Chapter 4.

(3-Bromomethylene-5-phenylpent-4-en-1-ynyl)trimethylsilane (259).*



Compound **259** was obtained as a white solid: $R_f = 0.2$ (hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.42 (m, 2H), 7.32 (m, 2H), 7.26 (m, 1H), 7.03 (d, $J = 15.6$ Hz, 1H), 6.71 (s, 1H), 6.66 (d, $J = 15.6$ Hz, 1H), 0.30 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 136.4, 133.0, 129.7, 128.8, 128.2, 126.9, 125.7, 115.9, 104.8, 98.9, -0.1 ; MS (EI, 70 eV) m/z 304.0/306.0 (M^+ , 27/28); HRMS m/z calcd for $\text{C}_{15}\text{H}_{17}\text{Si}^{79}\text{Br}/\text{C}_{15}\text{H}_{17}\text{Si}^{81}\text{Br}$ (M^+) 304.0283/306.0263, found 304.0277/306.0260. *TROESY (400 MHz, CDCl_3) spectrum is shown in Chapter 4.

Appendix A

X-Ray Crystallographic Data for Compound 211

University of Alberta Department of Chemistry
X-Ray Crystallography Laboratory

STRUCTURE REPORT

XCL Code: RRT0204
Date: 13 March 2002
Compound: 1,4-di(trimethylsilylbuta-1,3-diynyl)benzene
Formula: C₂₀H₂₂Si₂
Supervisor: R. R. Tykwinski
Crystallographer: M. J. Ferguson

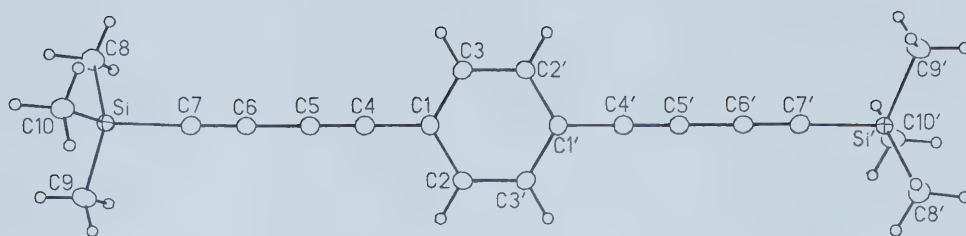


Figure 1. Perspective view of the 1,4-di(trimethylsilylbuta-1,3-diynyl)benzene molecule showing the atom labelling scheme. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.

Table 1. Crystallographic Experimental Details

A. Crystal Data

formula	C ₂₀ H ₂₂ Si ₂
formula weight	318.56
crystal dimensions (mm)	0.22 × 0.14 × 0.05
crystal system	triclinic
space group	<i>P</i> $\bar{1}$ (No. 2)
unit cell parameters ^a	
<i>a</i> (Å)	5.8635 (7)
<i>b</i> (Å)	6.0746 (7)
<i>c</i> (Å)	14.7262 (18)
α (deg)	87.686 (3)
β (deg)	80.087 (2)
γ (deg)	74.929 (2)
<i>V</i> (Å ³)	498.92 (10)
<i>Z</i>	1

ρ_{calcd} (g cm ⁻³)	1.060
μ (mm ⁻¹)	0.173

B. Data Collection and Refinement Conditions

diffractometer	Bruker PLATFORM/SMART 1000 CCDb
radiation (λ [Å])	graphite-monochromated Mo K α (0.71073)
temperature (°C)	−80
scan type	ω scans (0.2°) (25 s exposures)
data collection 2θ limit (deg)	52.82
total data collected	2729 (−7 (h (6, −7 (k (6, −18 (l (17)
independent reflections	2011 ($R_{\text{int}} = 0.0235$)
number of observed reflections (<i>NO</i>)	1505 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method	direct methods (<i>SHELXS</i> −86 ^c)
refinement method	full-matrix least-squares on F^2 (<i>SHELXL</i> −93 ^d)
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	0.9914–0.9629
data/restraints/parameters	2011 [$F_o^2 \geq -3\sigma(F_o^2)$] / 0 / 103
goodness-of-fit (<i>S</i>) ^e	1.037 [$F_o^2 \geq -3\sigma(F_o^2)$]
final <i>R</i> indices ^f	
<i>R</i> ₁ [$F_o^2 \geq 2\sigma(F_o^2)$]	0.0467
<i>wR</i> ₂ [$F_o^2 \geq -3\sigma(F_o^2)$]	0.1305
largest difference peak and hole	0.265 and −0.244 e Å ⁻³

^aObtained from least-squares refinement of 1096 reflections with $5.62^\circ < 2\theta < 50.97^\circ$.

(continued)

Table 1. Crystallographic Experimental Details (continued)

^bPrograms for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

^cSheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467–473.

^dSheldrick, G. M. *SHELXL-93*. Program for crystal structure determination. University of Göttingen, Germany, 1993. Refinement on F_o^2 for all reflections (all of these having $F_o^2 \geq -3\sigma(F_o^2)$). Weighted R -factors wR_2 and all goodnesses of fit S are based on F_o^2 ; conventional R -factors R_1 are based on F_o , with F_o set to zero for negative F_o^2 . The observed criterion of $F_o^2 > 2\sigma(F_o^2)$ is used only for calculating R_1 , and is not relevant to the choice of reflections for refinement. R -factors based on F_o^2 are statistically about twice as large as those based on F_o , and R -factors based on ALL data will be even larger.

^e $S = [\Sigma w(F_o^2 - F_c^2)^2 / (n - p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [\sigma^2(F_o^2) + (0.0758P)^2]^{-1}$ where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$).

^f $R_1 = \Sigma ||F_o| - |F_c|| / \Sigma |F_o|$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2 / \Sigma w(F_o^4)]^{1/2}$.

Table 2. Atomic Coordinates and Equivalent Isotropic Displacement Parameters

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq} , Å ²
Si	0.59019(11)	0.74793(10)	0.32511(4)	0.0369(2)*
C1	0.0947(4)	0.1222(3)	0.05529(14)	0.0381(5)*
C2	0.2144(4)	-0.1040(4)	0.02970(15)	0.0397(5)*
C3	-0.1201(4)	0.2232(4)	0.02469(15)	0.0395(5)*
C4	0.1927(4)	0.2458(4)	0.11270(15)	0.0410(5)*
C5	0.2767(4)	0.3504(4)	0.15927(16)	0.0419(5)*
C6	0.3768(4)	0.4715(4)	0.21119(16)	0.0414(5)*
C7	0.4634(4)	0.5787(4)	0.25685(16)	0.0434(6)*
C8	0.3331(5)	0.9526(4)	0.39395(18)	0.0588(7)*
C9	0.7756(5)	0.5481(4)	0.39862(18)	0.0569(7)*
C10	0.7751(4)	0.8988(4)	0.2450(2)	0.0567(7)*

Anisotropically-refined atoms are marked with an asterisk (*). The form of the anisotropic displacement parameter is: $\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^{*}c^{*}U_{23} + 2hla^{*}c^{*}U_{13} + 2hka^{*}b^{*}U_{12})]$.

Table 3. Selected Interatomic Distances (Å)

Atom1	Atom2	Distance	Atom1	Atom2	Distance
Si	C7	1.832(2)	C1	C4	1.432(3)
Si	C8	1.857(2)	C2	C3'	1.371(3) [†]
Si	C9	1.855(2)	C2	C3'	1.371(3) [†]
Si	C10	1.843(3)	C4	C5	1.196(3)
C1	C2	1.404(3)	C5	C6	1.377(3)
C1	C3	1.392(3)	C6	C7	1.208(3)

Table 4. Selected Interatomic Angles (deg)

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle	
C7	Si	C8	106.66(11)		C3	C1	C4	120.71(19)
C7	Si	C9	107.58(11)	C1	C2	C3'	120.2(2) [†]	
C7	Si	C10	108.17(12)	C1	C3	C2'	120.61(19) [†]	
C8	Si	C9	112.36(12)	C1	C4	C5	178.8(2)	
C8	Si	C10	111.00(13)	C4	C5	C6	178.7(2)	
C9	Si	C10	110.83(12)	C5	C6	C7	179.6(2)	
C2	C1	C3	119.2(2)	Si	C7	C6	178.57(19)	
C2	C1	C4	120.1(2)					

Table 5. Torsional Angles (deg)

Atom1	Atom2	Atom3	Atom4	Angle	Atom1	Atom2	Atom3	Atom4	Angle
C8	Si	C7	C6	51(9)	C2	C1	C4	C5	90(11)
C9	Si	C7	C6	172(9)	C3	C1	C4	C5	-90(11)
C10	Si	C7	C	- 68(9)	C1	C2	C3'	C1'	0.0(4) [†]
C3	C1	C2	C3'	0.0(4) [†]	C1	C4	C5	C6	-12(20)
C4	C1	C2	C3'	179.5(2) [†]	C4	C5	C6	C7	117(37)
C2	C1	C3	C2'	0.0(4) [†]	C5	C6	C7	Si	-35(45)
C4	C1	C3	C2'	-179.5(2) [†]					

[†]Primed atoms are related to unprimed atoms by the crystallographic inversion centre (0, 0, 0).

Table 6. Anisotropic Displacement Parameters (U_{ij} , Å²)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Si	0.0349(4)	0.0344(3)	0.0401(4)	-0.0032(2)	-0.0099(2)	-0.0039(2)
C1	0.0396(12)	0.0399(12)	0.0356(11)	0.0007(9)	-0.0046(9)	-0.0131(9)
C2	0.0361(12)	0.0391(12)	0.0426(12)	0.0031(9)	-0.0081(10)	-0.0069(9)
C3	0.0403(12)	0.0340(11)	0.0423(12)	-0.0014(9)	-0.0040(10)	-0.0080(9)
C4	0.0403(13)	0.0409(12)	0.0408(12)	-0.0010(10)	-0.0055(10)	-0.0091(10)
C5	0.0399(13)	0.0401(12)	0.0438(13)	-0.0039(10)	-0.0082(10)	-0.0056(10)
C6	0.0385(12)	0.0366(12)	0.0468(13)	-0.0029(10)	-0.0092(10)	-0.0038(9)
C7	0.0414(13)	0.0382(12)	0.0483(13)	-0.0047(10)	-0.0075(11)	-0.0056(10)
C8	0.0518(16)	0.0600(16)	0.0564(16)	-0.0167(13)	-0.0084(13)	0.0020(12)
C9	0.0523(16)	0.0598(16)	0.0534(15)	0.0070(12)	-0.0154(13)	-0.0022(12)
C10	0.0459(15)	0.0457(14)	0.0761(18)	0.0115(13)	-0.0100(13)	-0.0096(11)

The form of the anisotropic displacement parameter is:
 $\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^{*c^{*}}U_{23} + 2hla^{*c^{*}}U_{13} + 2hka^{*b^{*}}U_{12})]$

Table 7. Derived Atomic Coordinates and Displacement Parameters for Hydrogen Atoms

Atom	x	y	z	U_{eq} , Å ²
H2	0.3612	-0.1746	0.0501	0.048
H3	-0.2021	0.3762	0.0417	0.047
H8A	0.2293	1.0414	0.3527	0.088
H8B	0.3926	1.0558	0.4277	0.088
H8C	0.2416	0.8688	0.4378	0.088
H9A	0.9070	0.4420	0.3594	0.085
H9B	0.6762	0.4622	0.4376	0.085
H9C	0.8415	0.6344	0.4376	0.085
H10A	0.9097	0.7874	0.2097	0.085
H10B	0.8364	0.9979	0.2800	0.085
H10C	0.6774	0.9912	0.2026	0.085

Appendix B

^1H and ^{13}C NMR Spectra for di- and triynes synthesized.

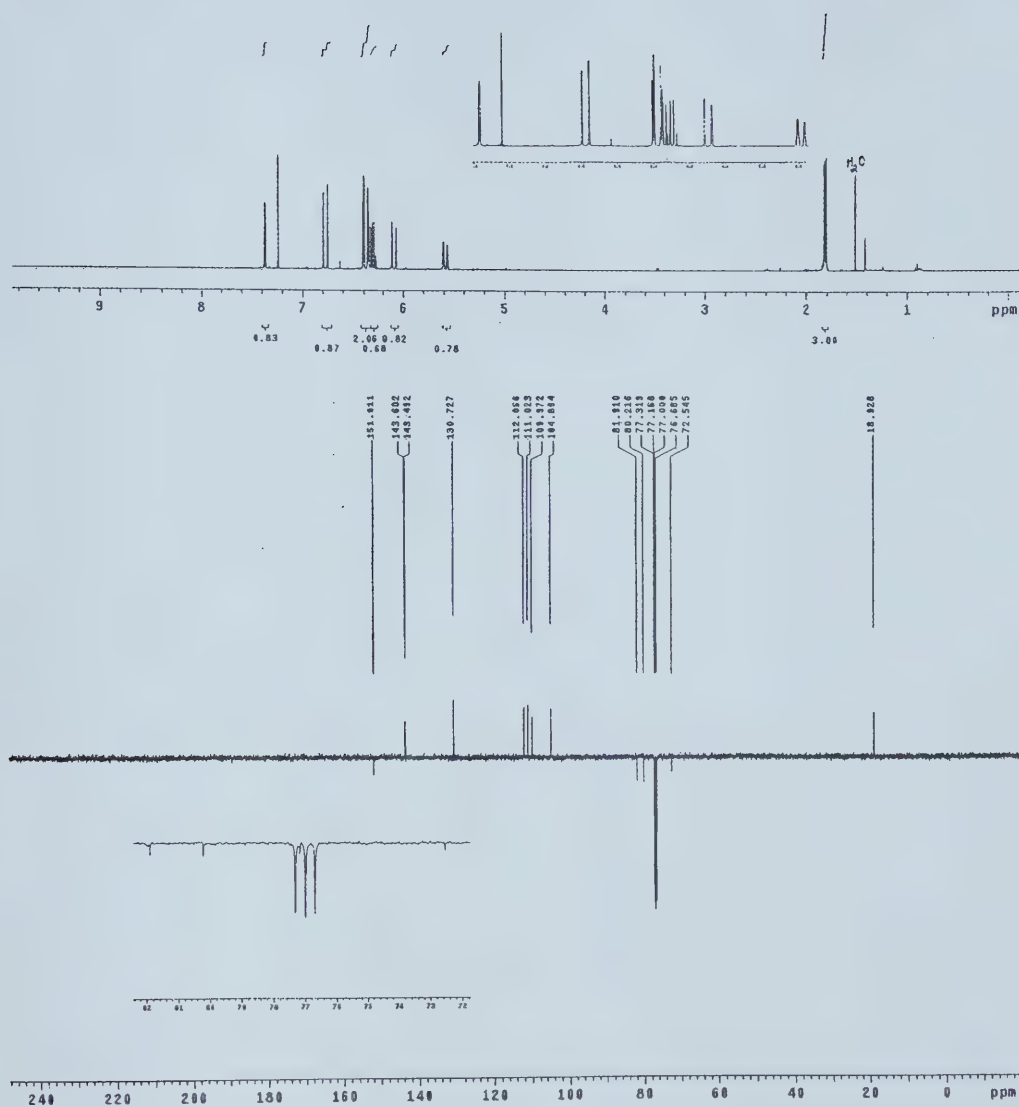


Figure B1. ^1H and ^{13}C NMR spectra for compound 12.

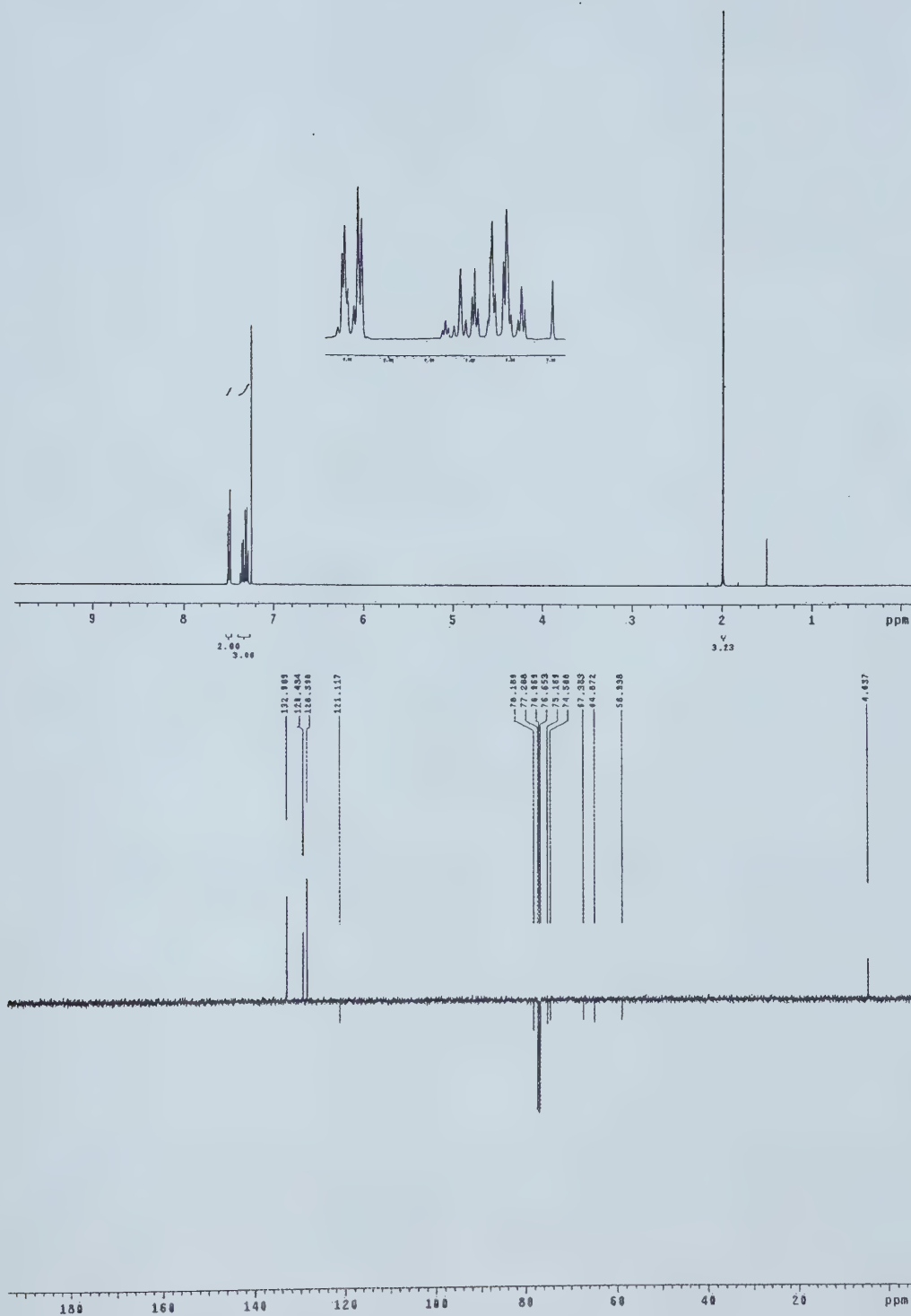


Figure B2. ^1H and ^{13}C NMR spectra for compound 167.

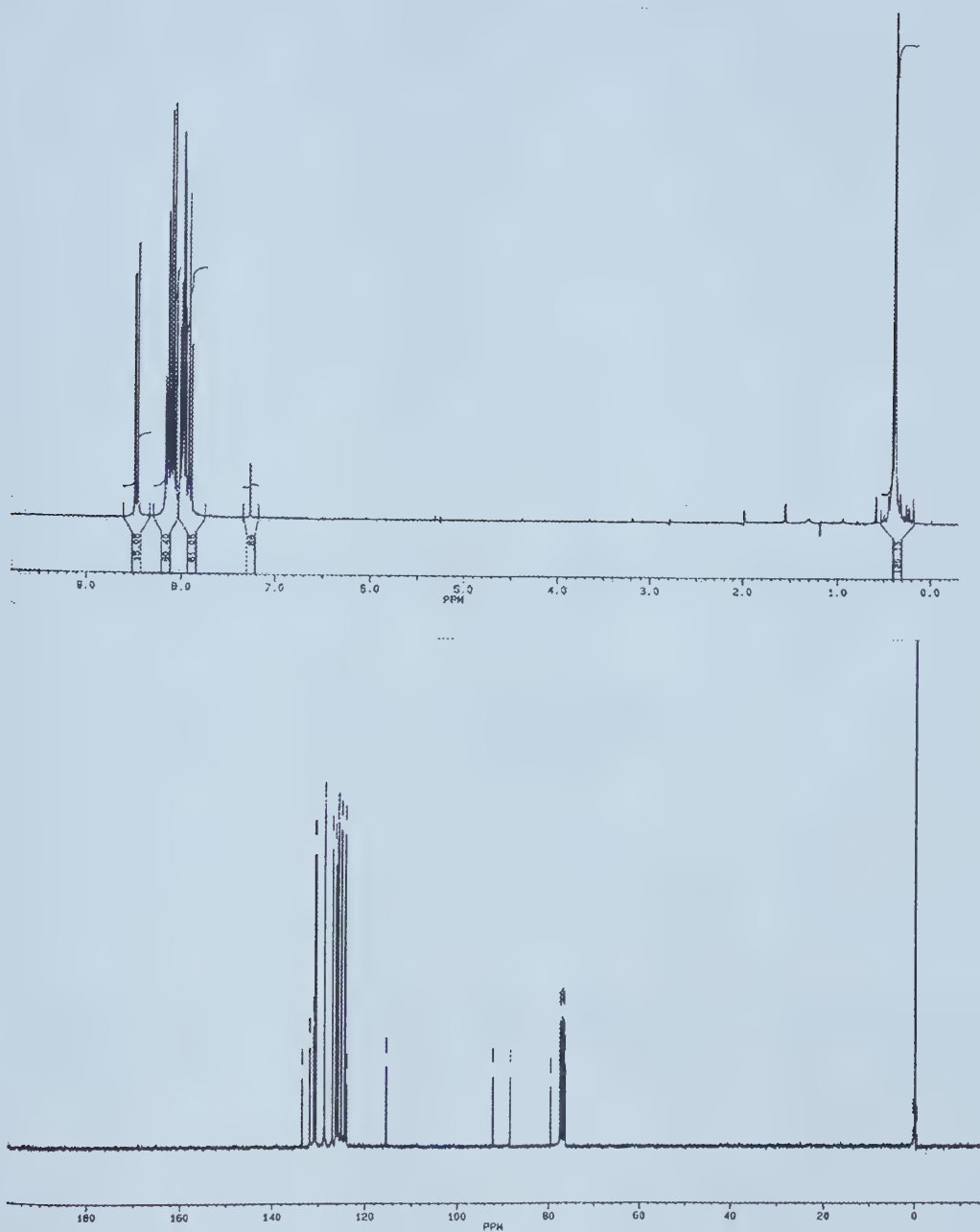


Figure B4. ^1H and ^{13}C NMR spectra for compound 201b.

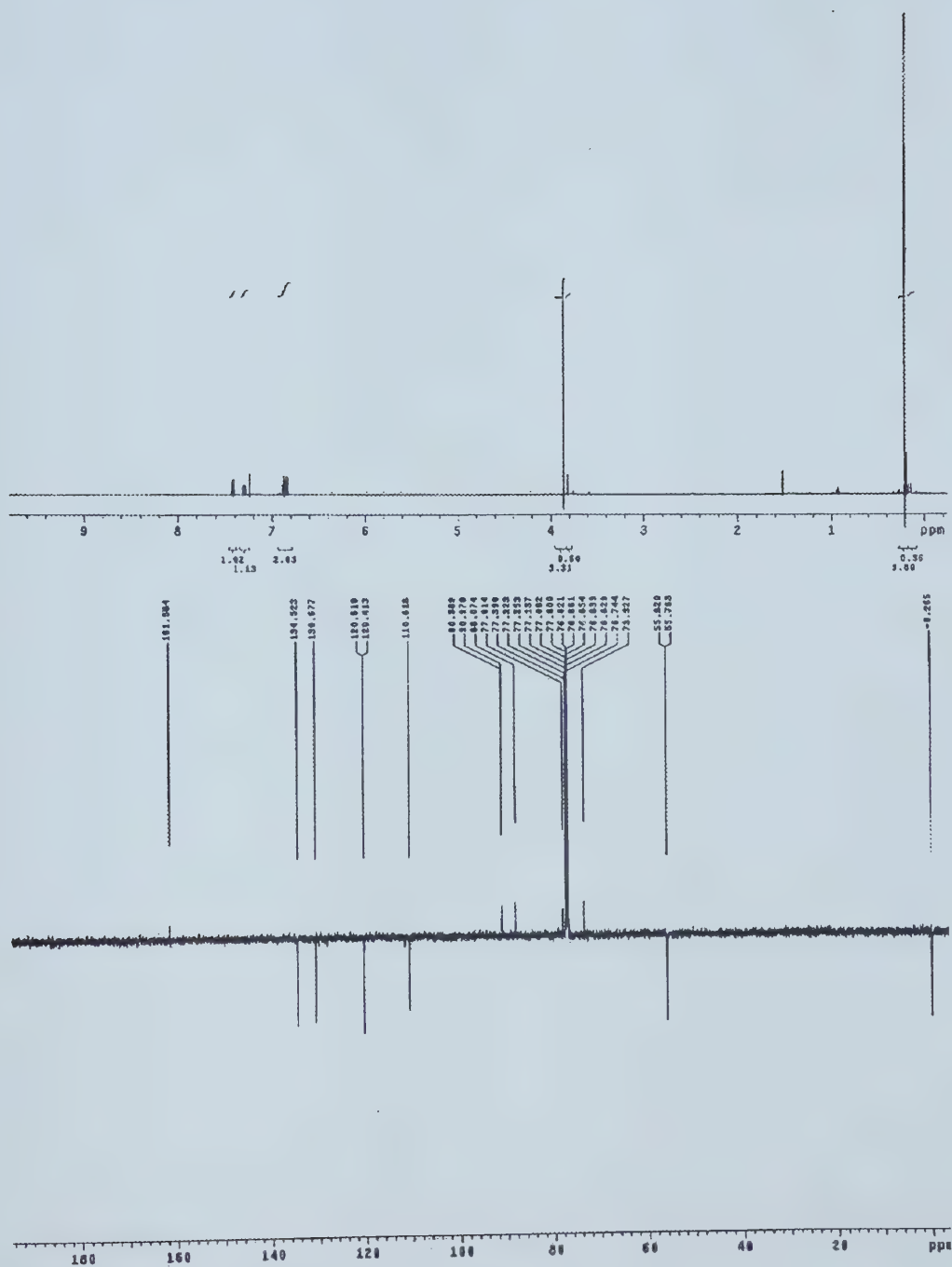


Figure B5. ¹H and ¹³C NMR spectra for compound 201c.



Figure B6. ¹H and ¹³C NMR spectra for compound 21d.

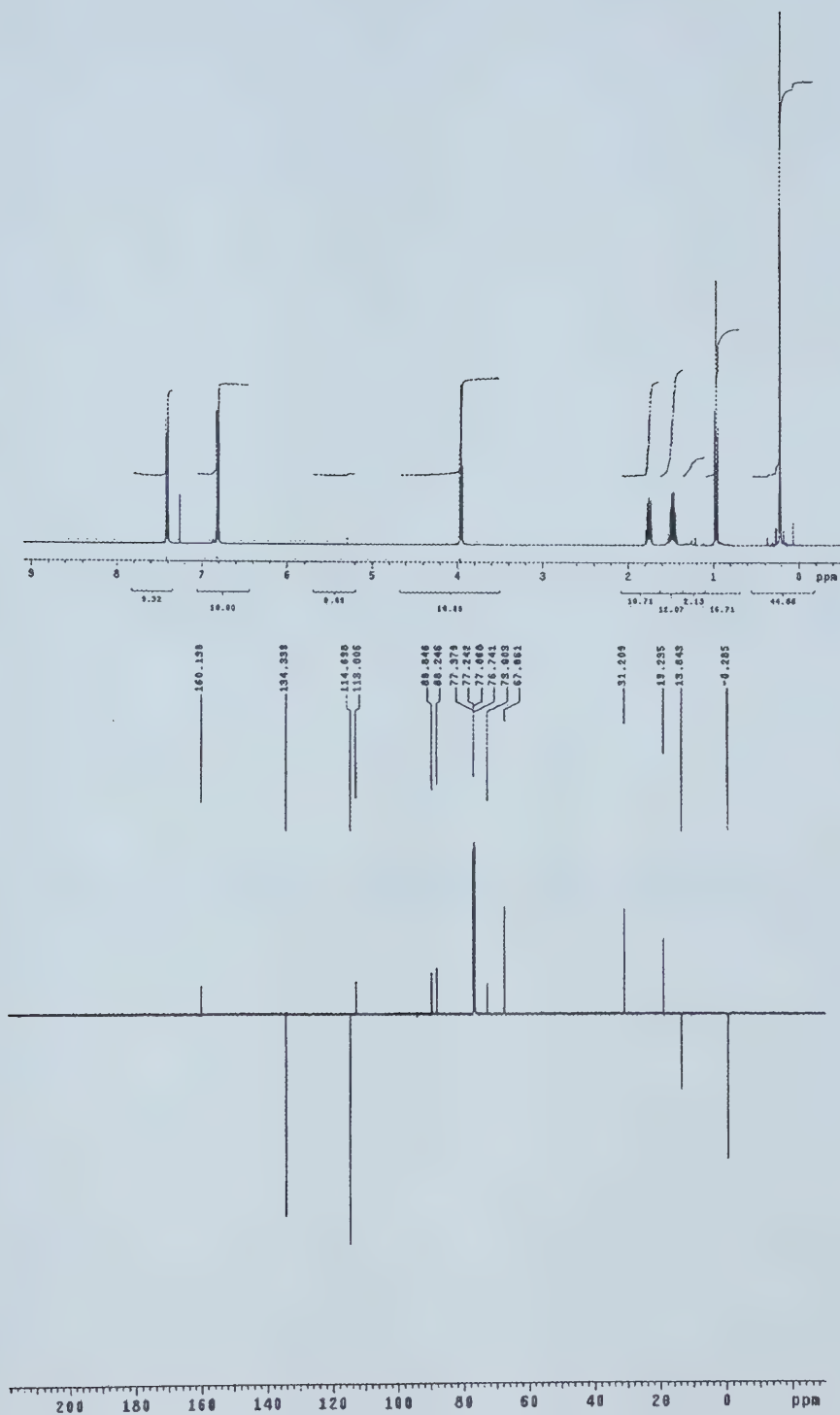


Figure B7. ^1H and ^{13}C NMR spectra for compound 201f.

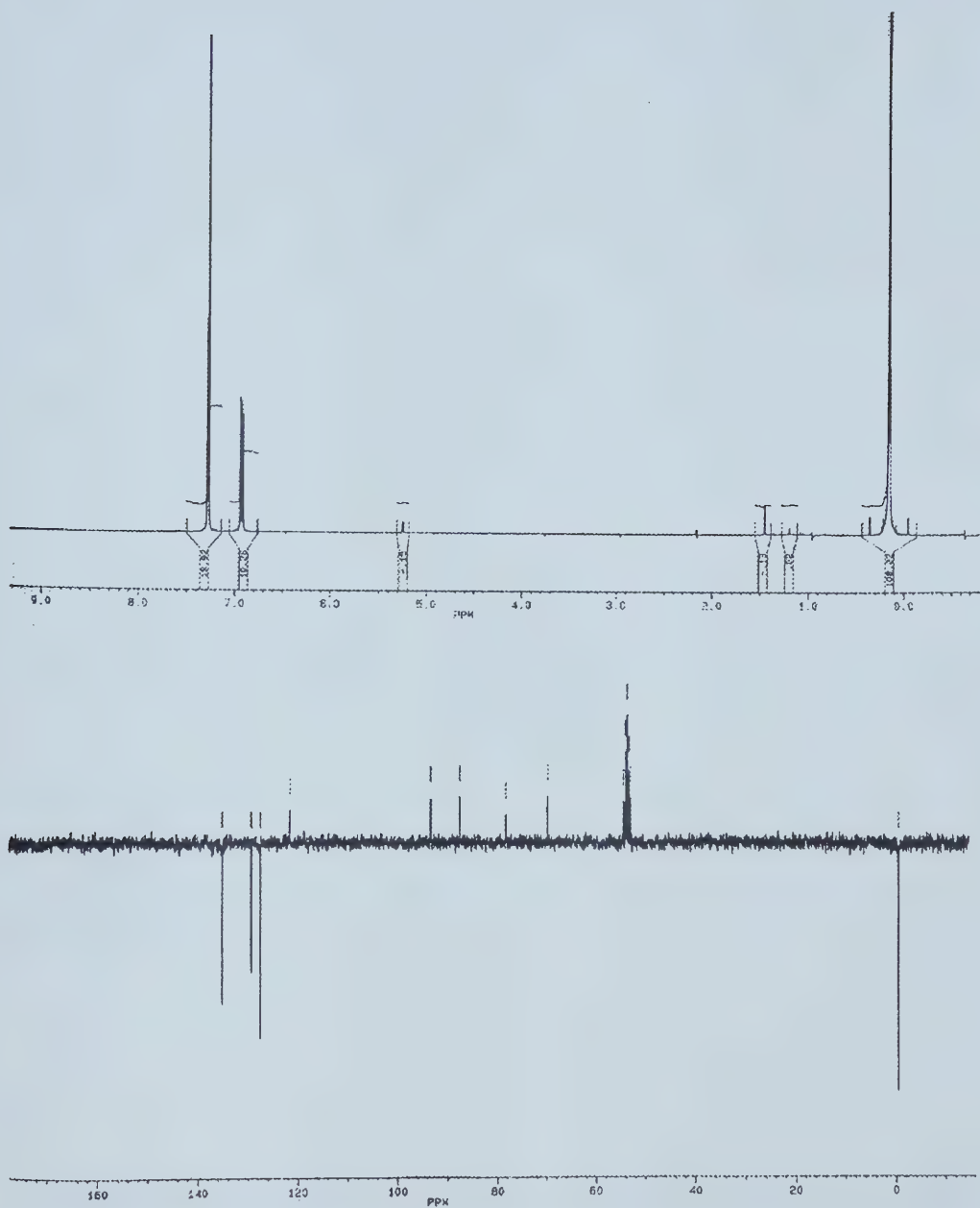
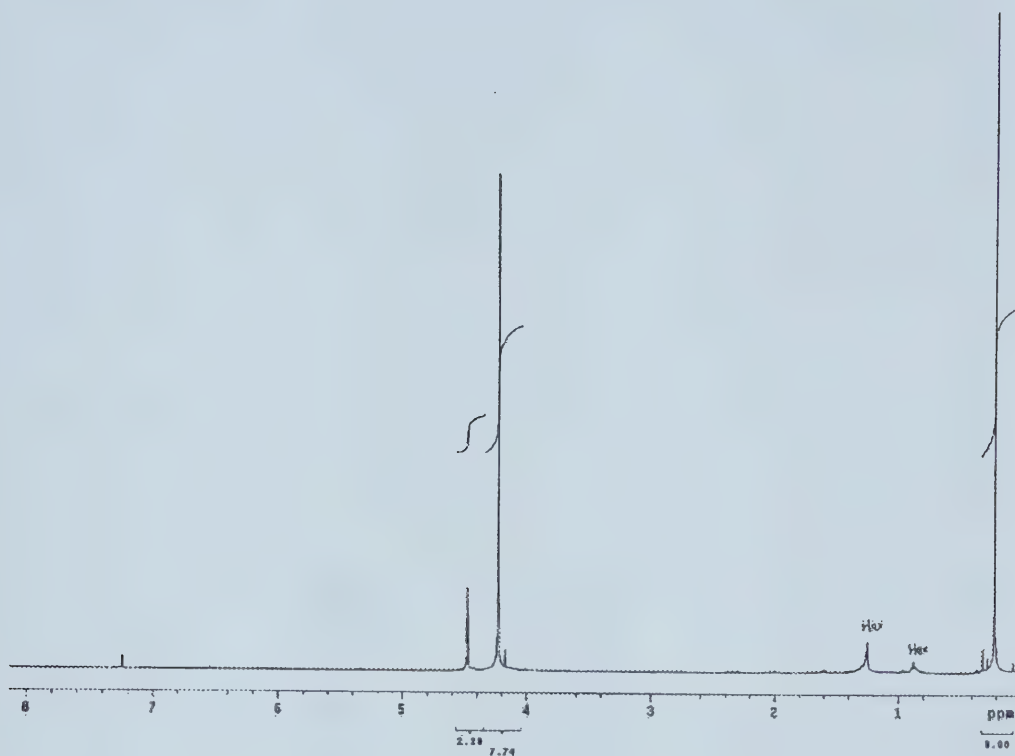


Figure B9. ^1H and ^{13}C NMR spectra for compound 201i.



INDEX	FREQUENCY	PPM	HEIGHT
1	8314.788	86.671	~10.0
2	8002.177	87.558	~7.2
3	7774.624	77.324	~9.4
4	7770.972	77.294	~12.3
5	7738.928	76.978	~12.5
6	7706.884	76.866	~13.3
7	7269.668	72.368	18.7
8	7030.725	70.528	~5.7
9	7052.272	70.149	70.6
10	6973.538	69.982	31.4
11	6287.185	62.585	~6.0
12	~35.544	~0.354	21.2

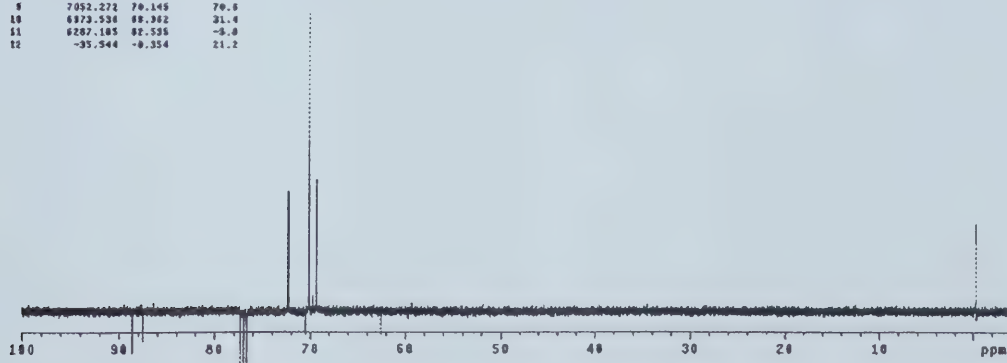


Figure B10. ^1H and ^{13}C NMR spectra for compound 201k.

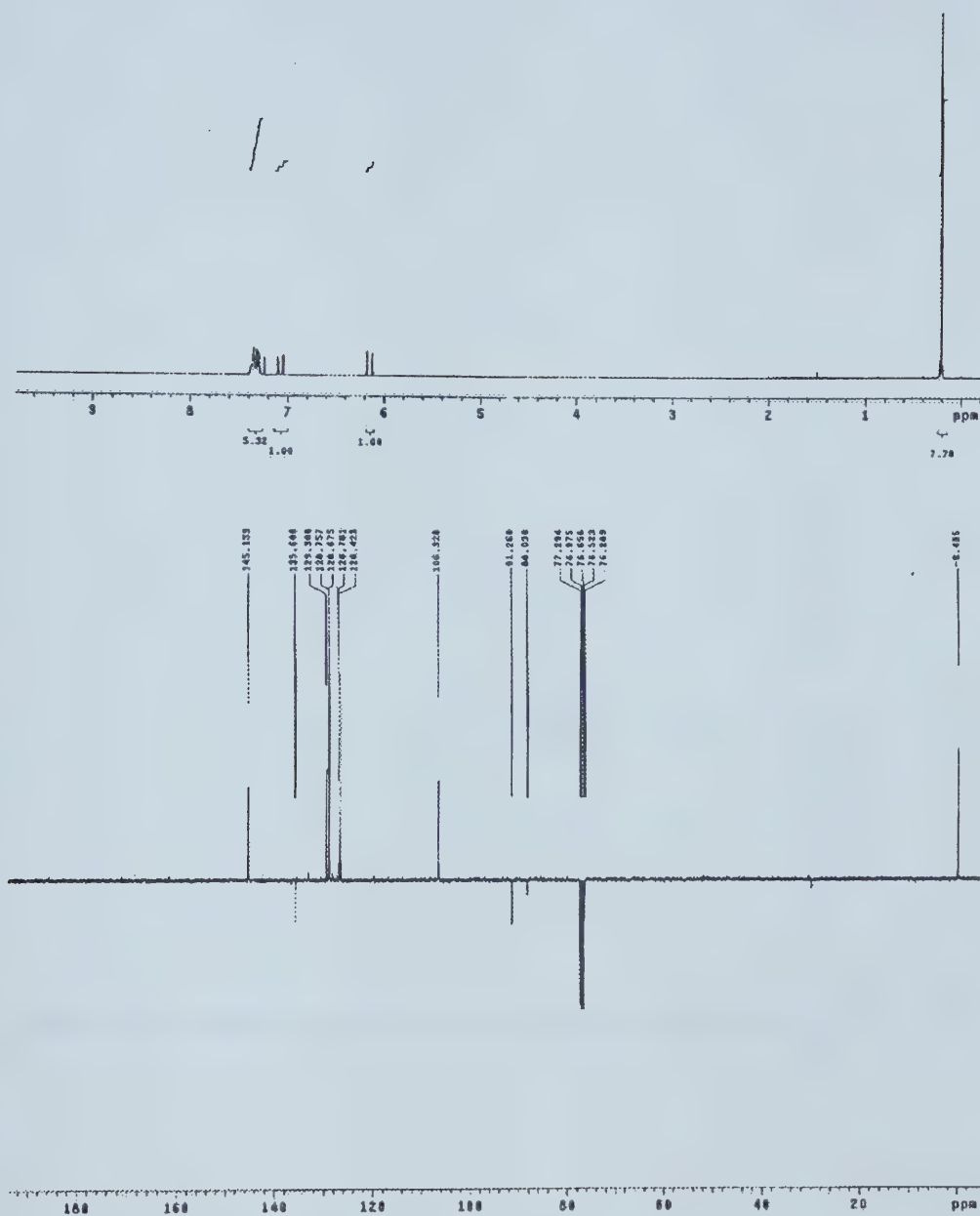


Figure B11. ¹H and ¹³C NMR spectra for compound 201l.

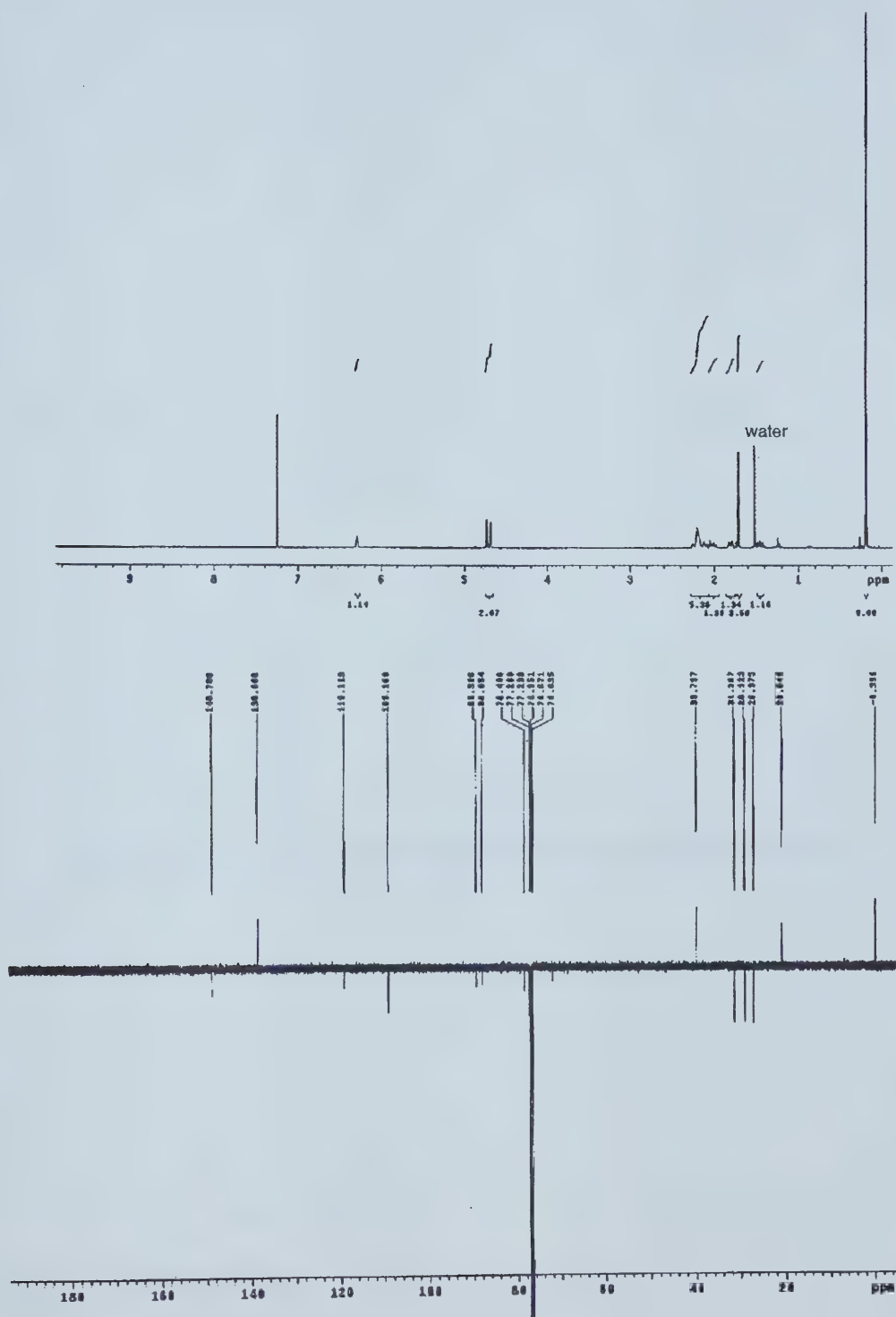


Figure B12. ^1H and ^{13}C NMR spectra for compound 201m.

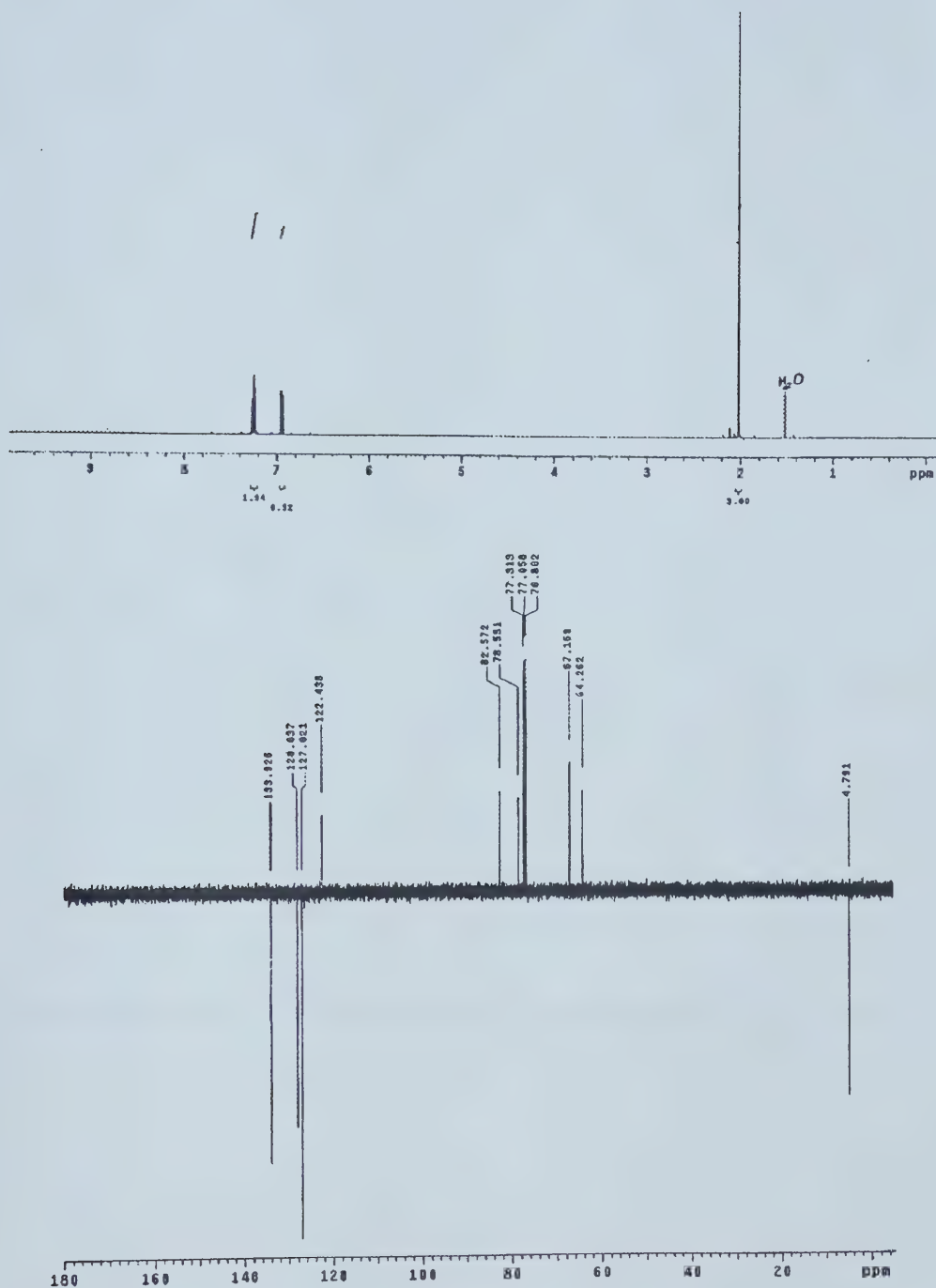


Figure B13. ¹H and ¹³C NMR spectra for compound 201r.



Figure B14. ^1H and ^{13}C NMR spectra for compound 204a.

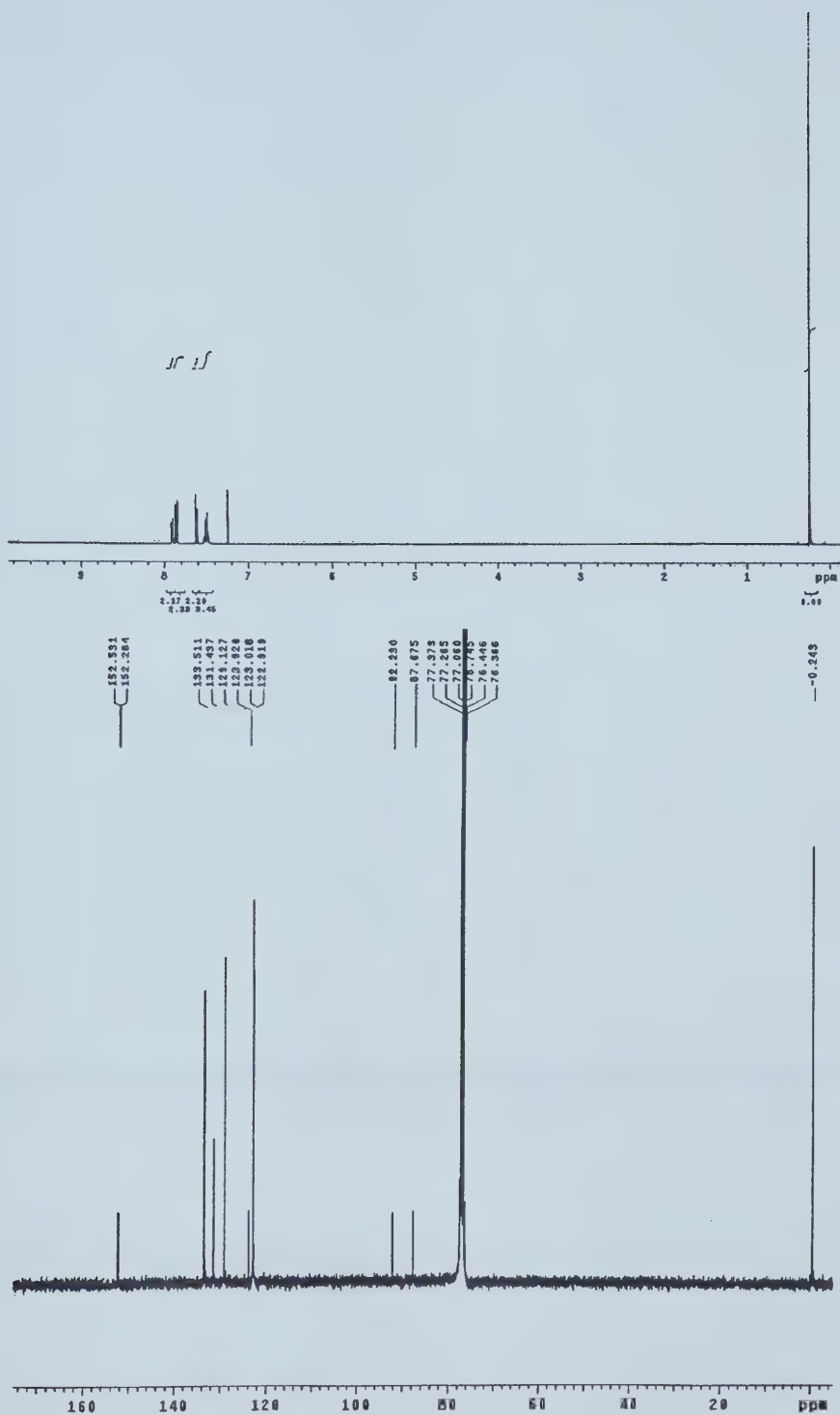


Figure B15. ¹H and ¹³C NMR spectra for compound 204c.

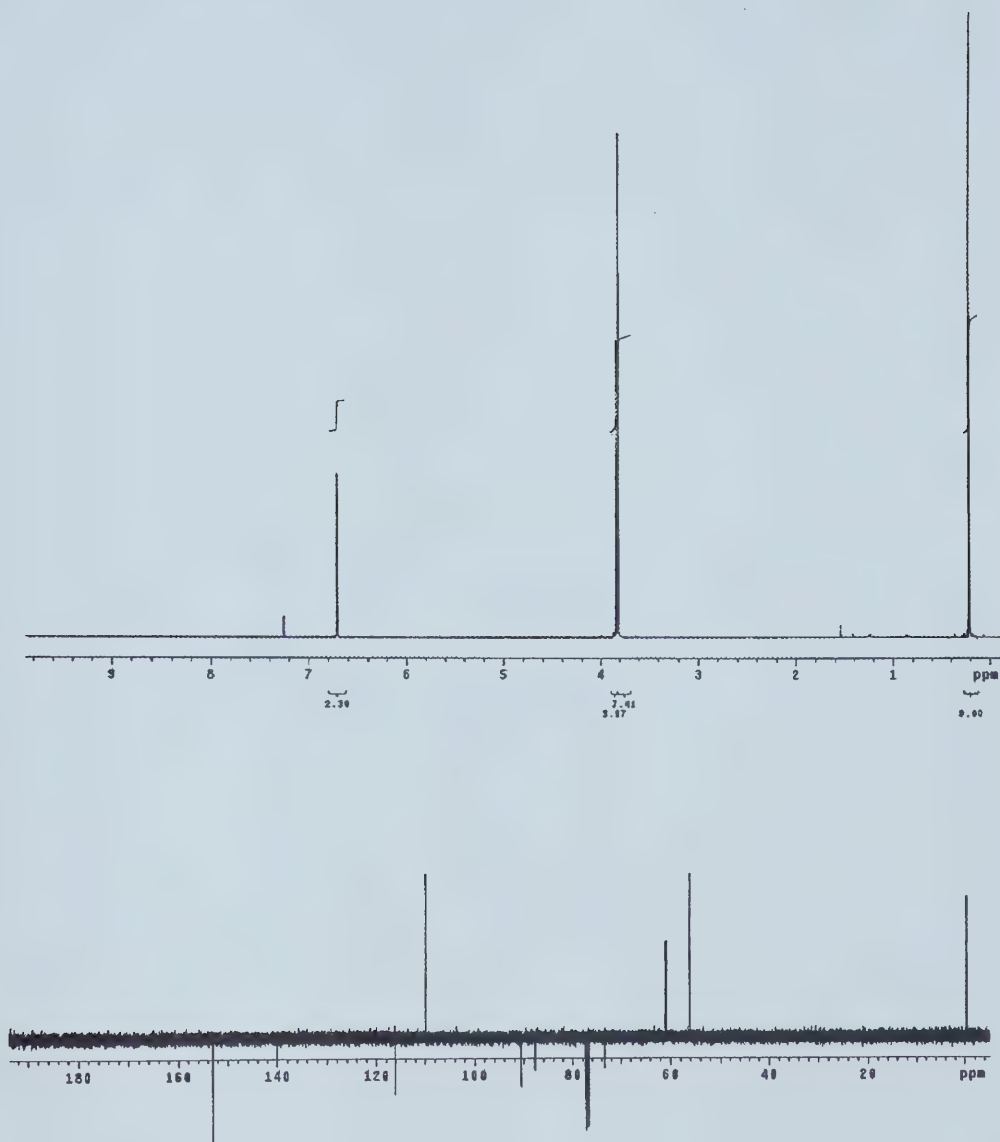


Figure B16. ^1H and ^{13}C NMR spectra for compound 204d.

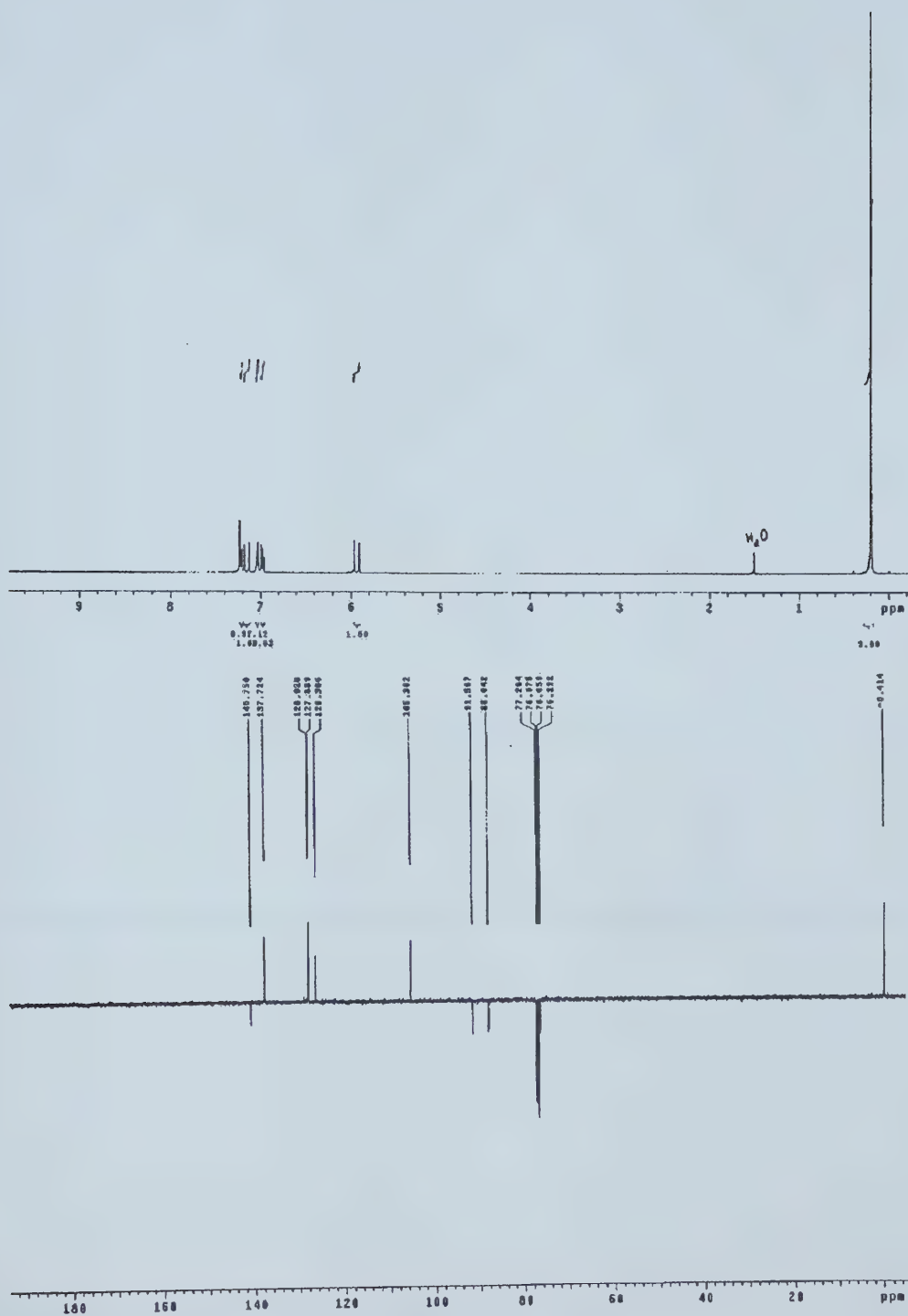


Figure B17. ¹H and ¹³C NMR spectra for compound 204e.

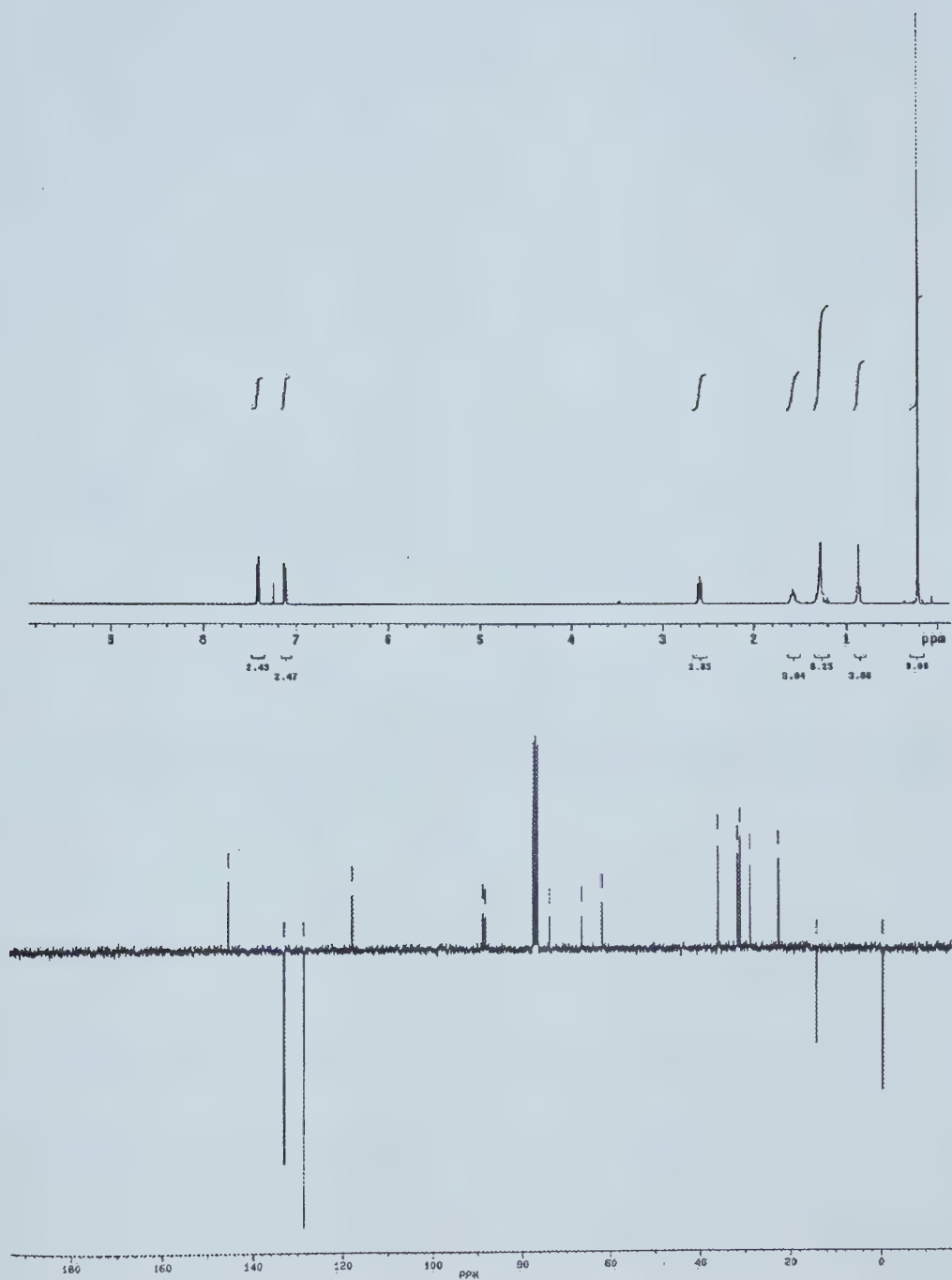


Figure B18. ^1H and ^{13}C NMR spectra for compound 207a.

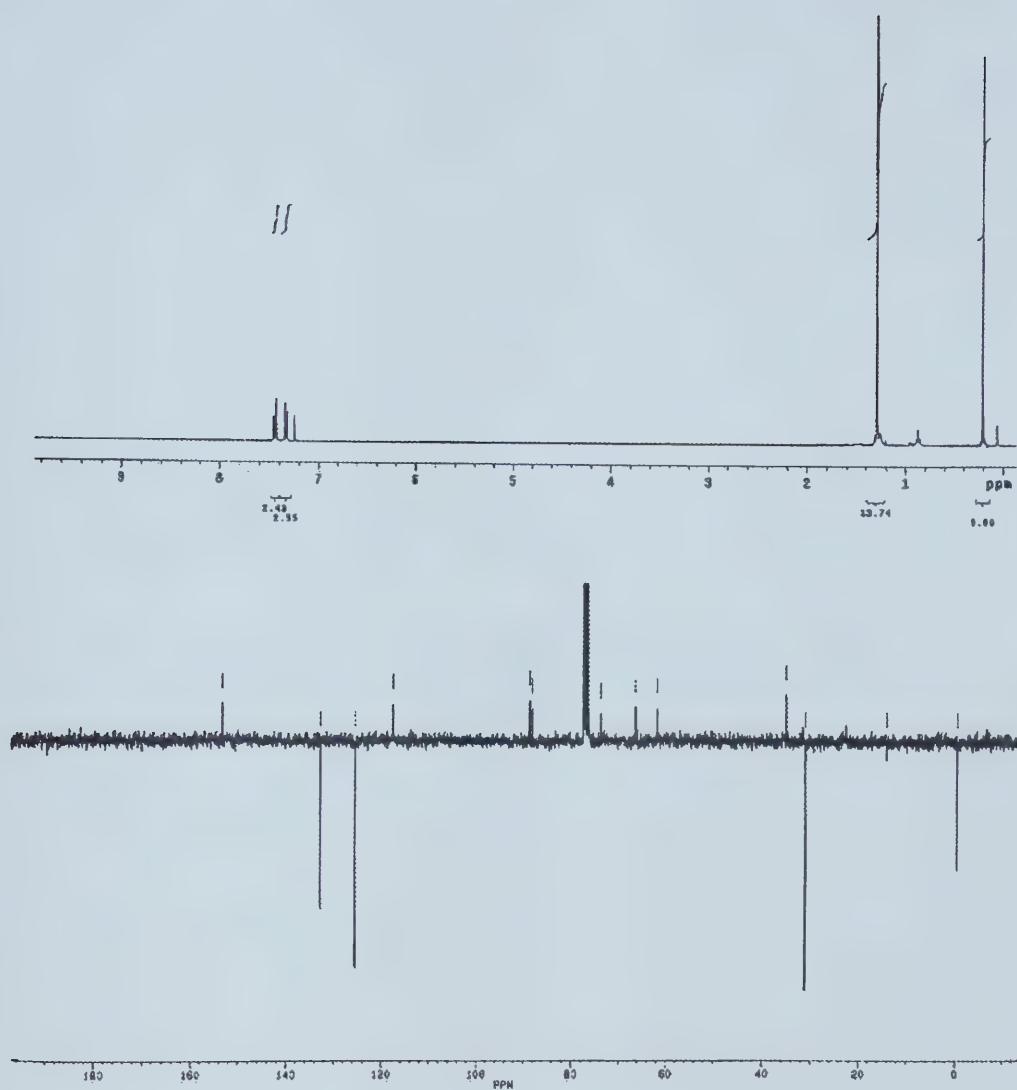


Figure B19. ^1H and ^{13}C NMR spectra for compound 207b.

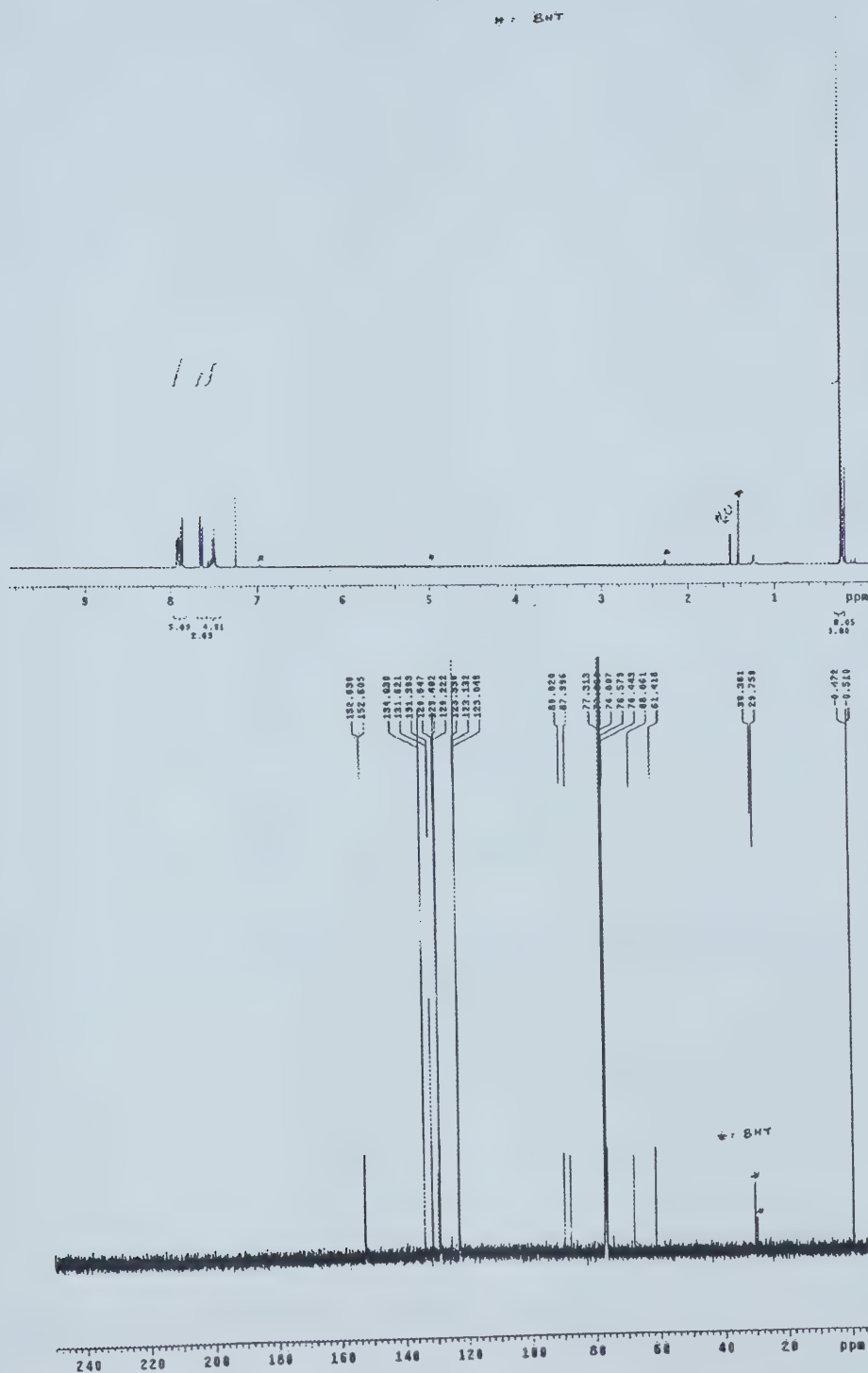


Figure B20. ¹H and ¹³C NMR spectra for compound 207c.

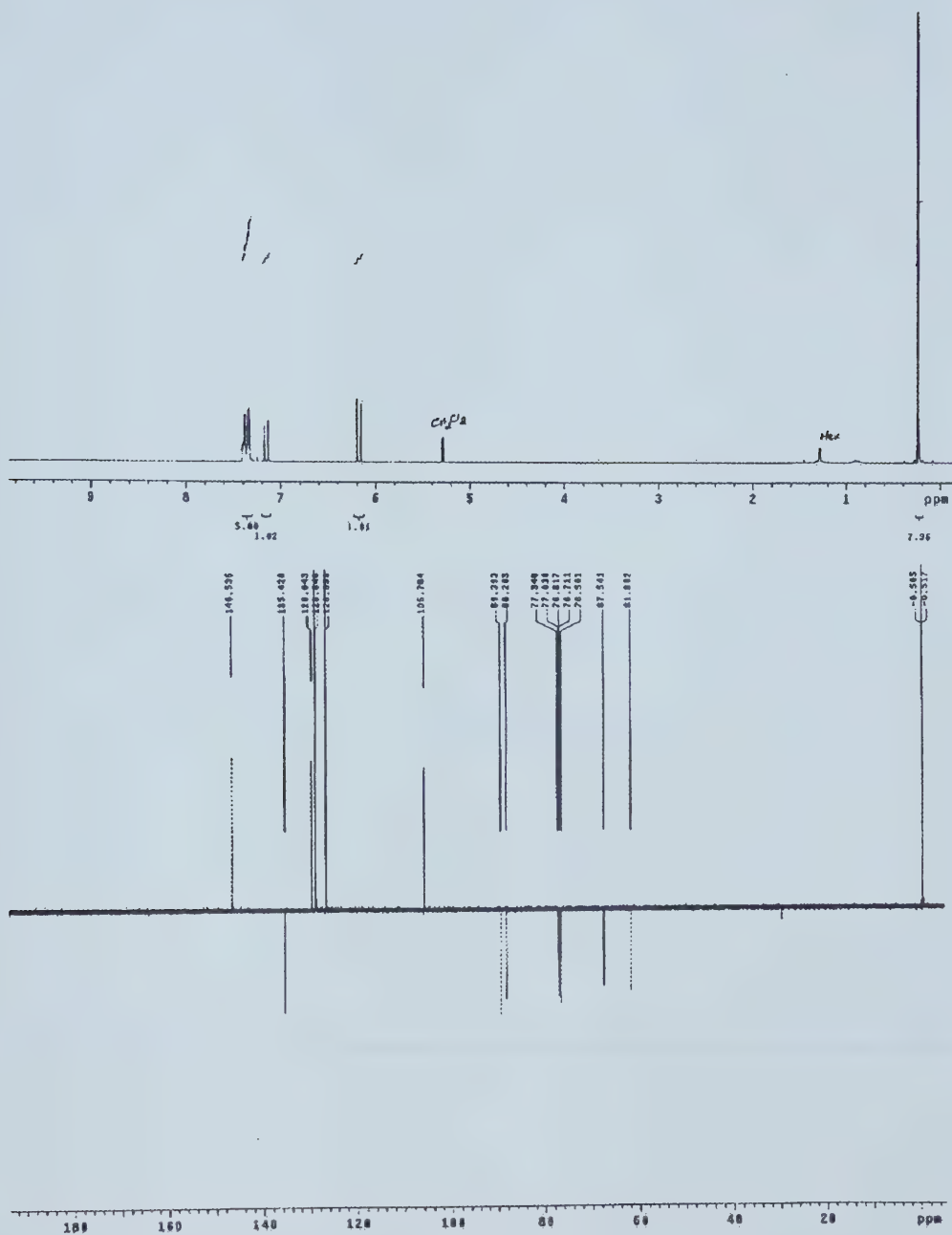
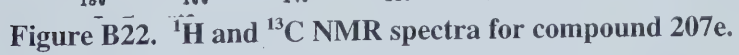


Figure B21. ¹H and ¹³C NMR spectra for compound 207d.



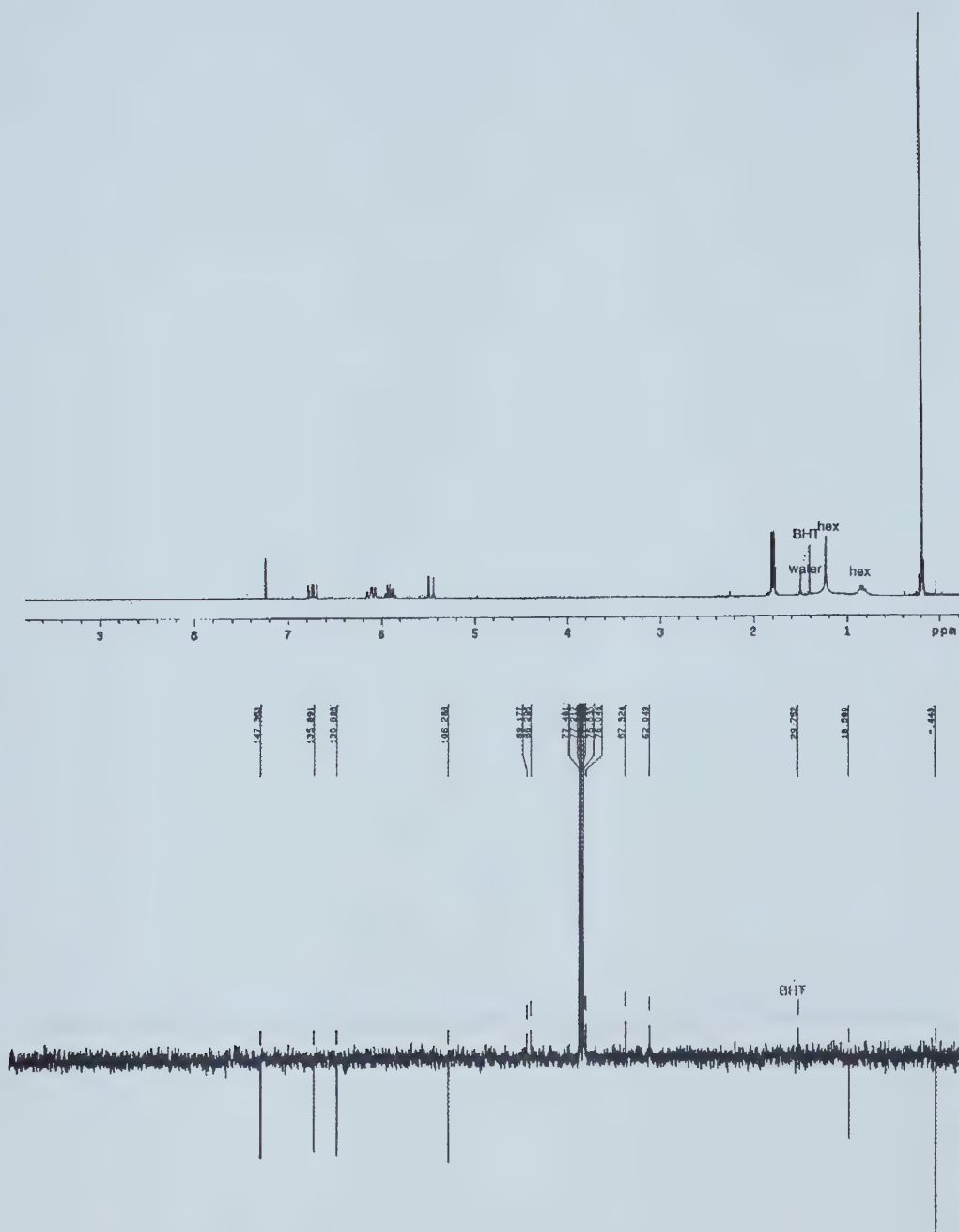


Figure B23. ^1H and ^{13}C NMR spectra for compound 207f.

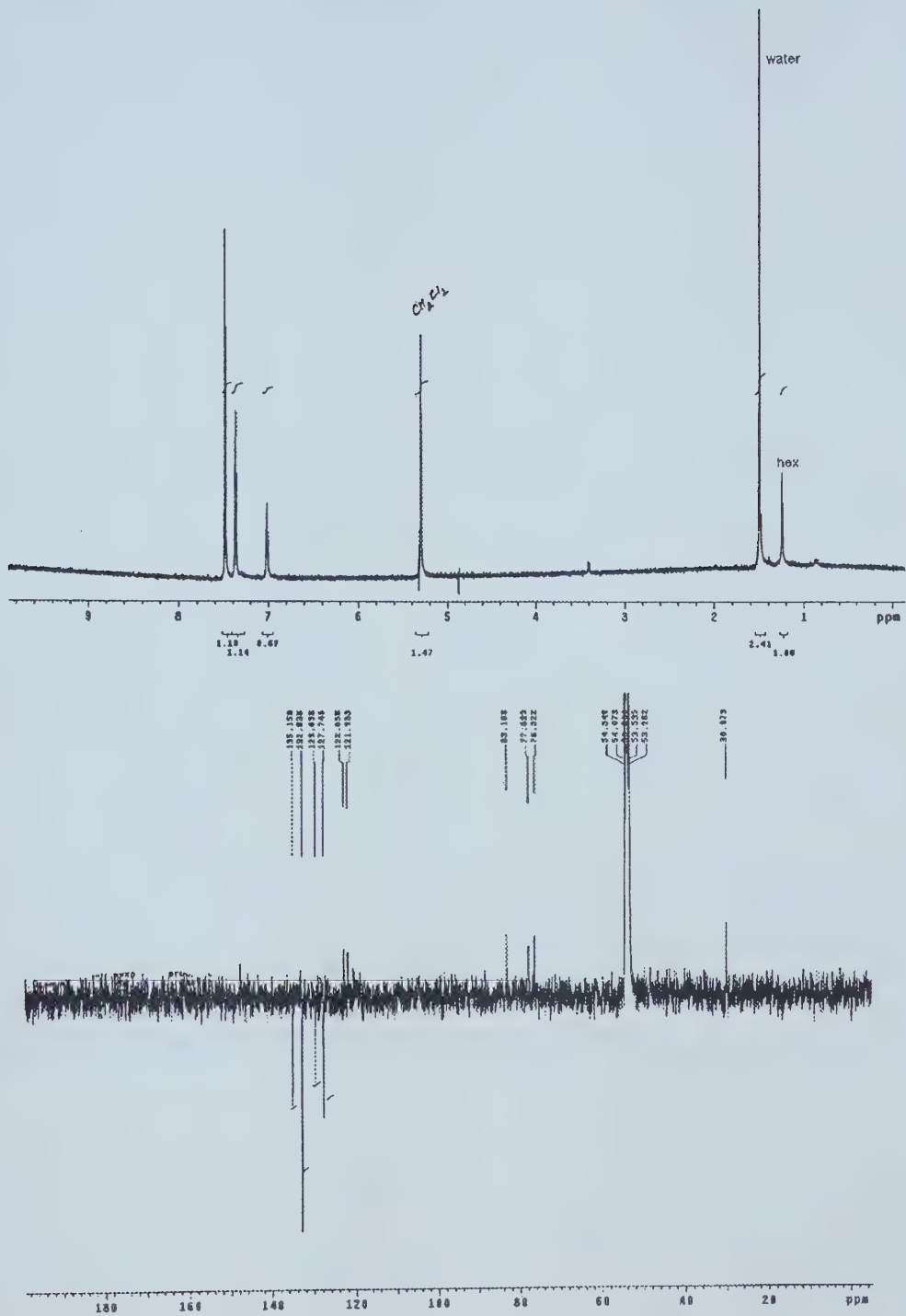


Figure B25. ¹H and ¹³C NMR spectra for compound 214.

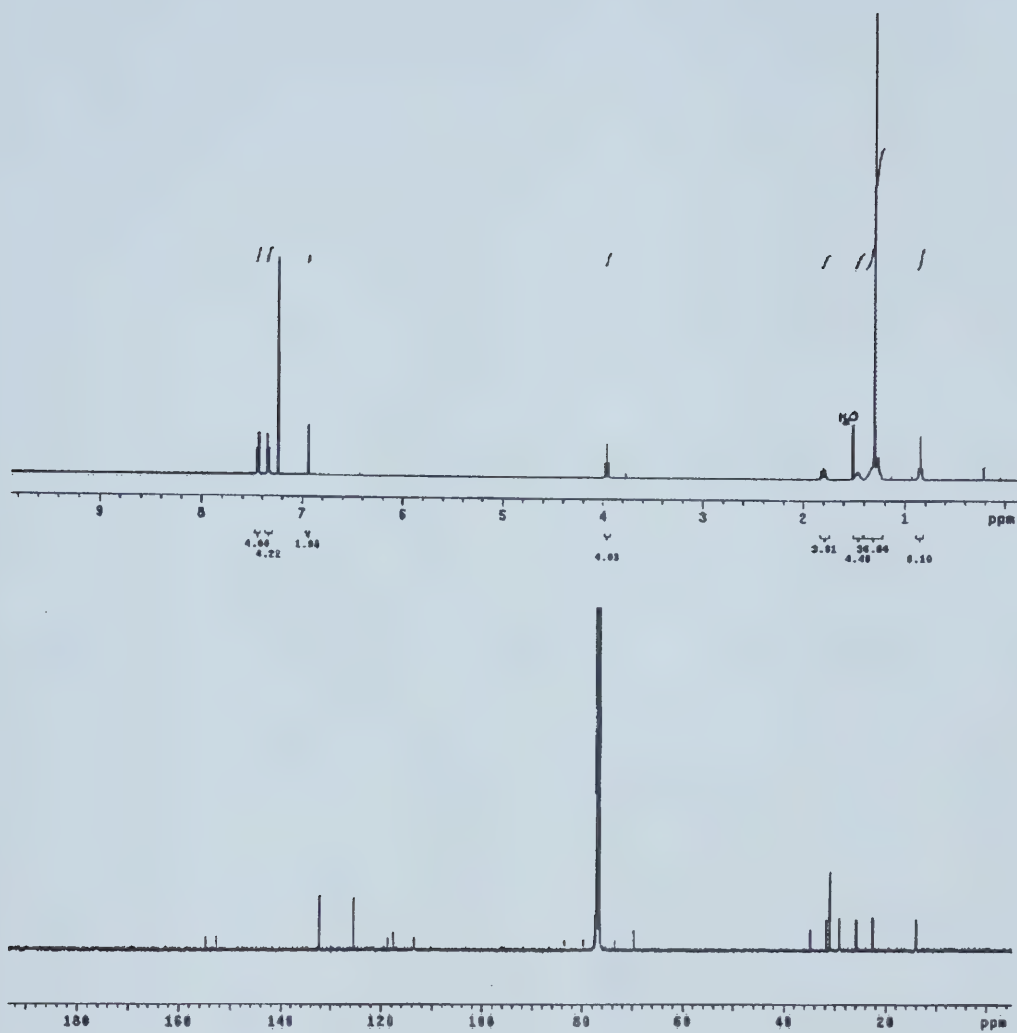


Figure B26. ^1H and ^{13}C NMR spectra for compound 215.



Figure B27. ¹H and ¹³C NMR spectra for compound 216.

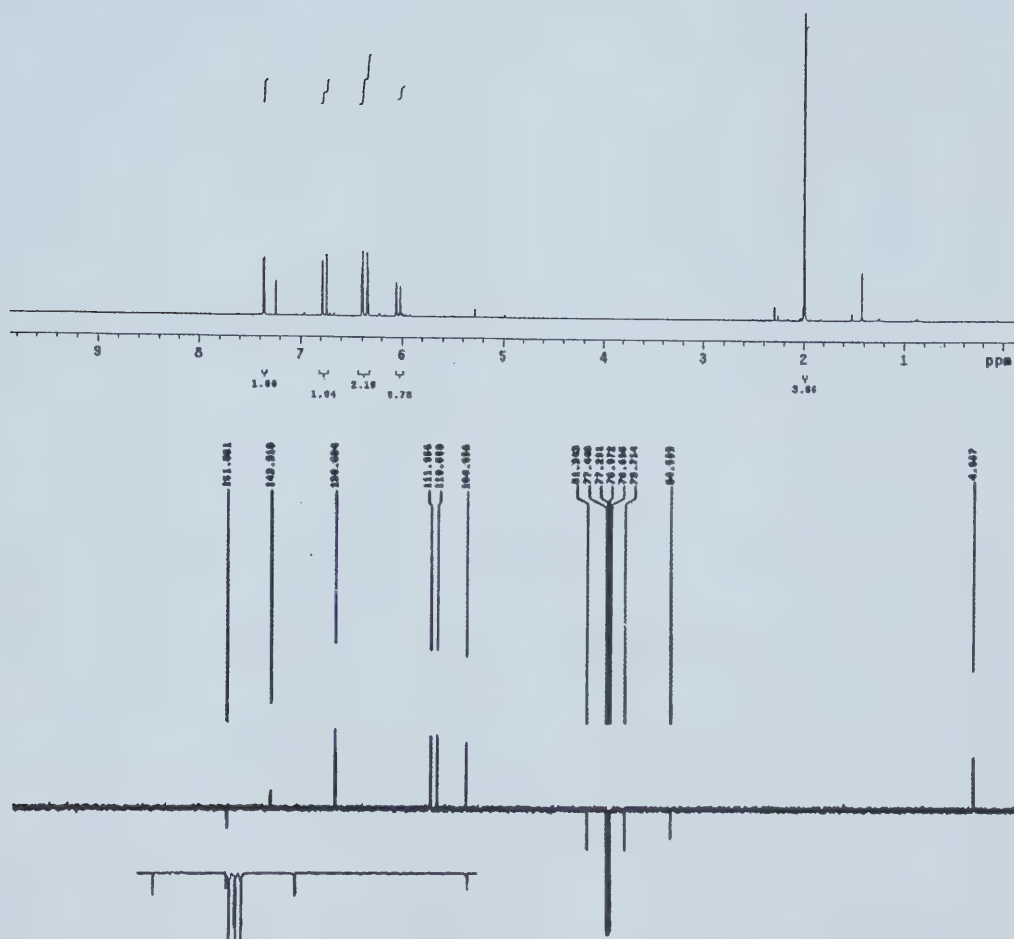


Figure B28. ^1H and ^{13}C NMR spectra for compound 217.

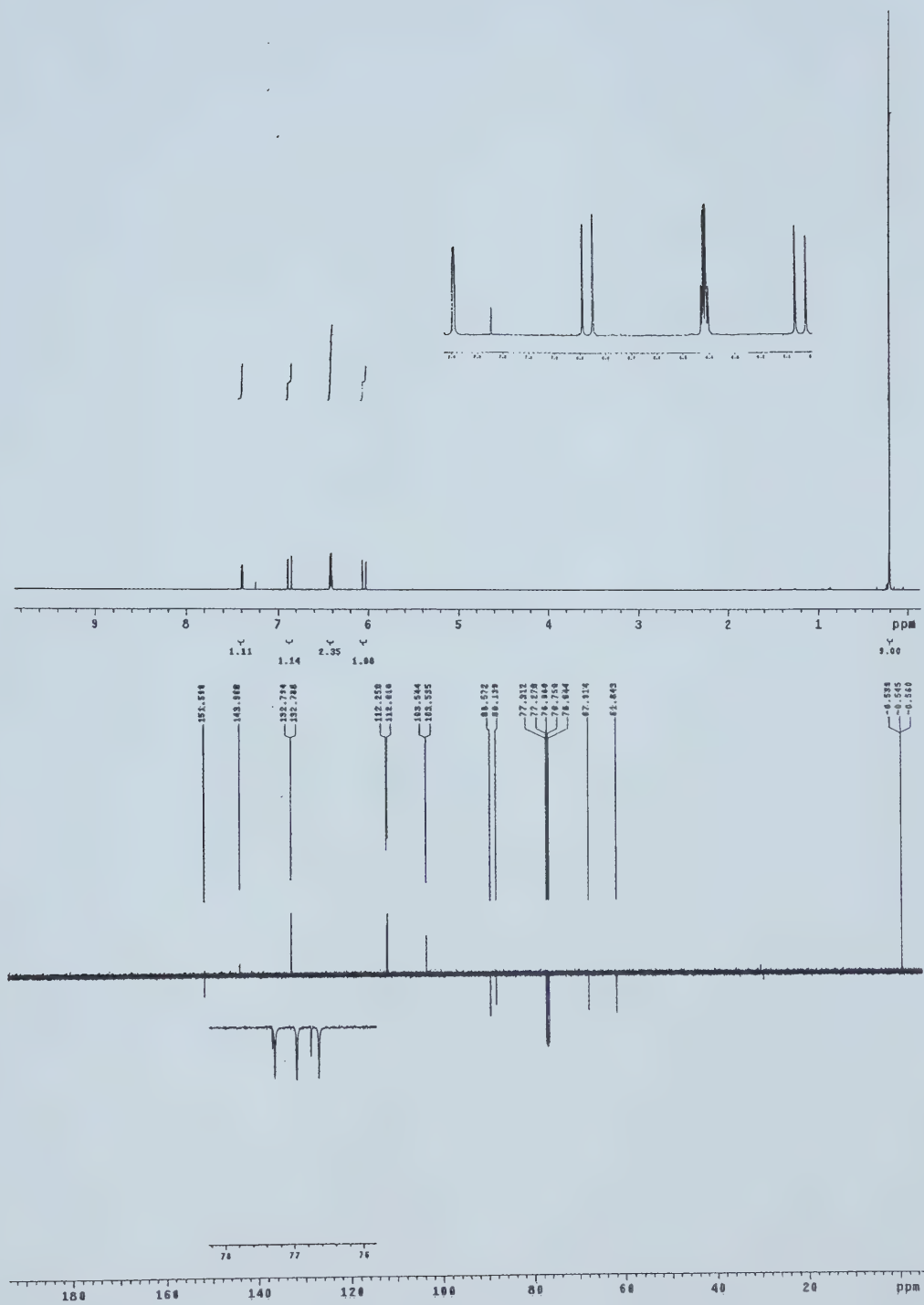




Figure B30. ^1H and ^{13}C NMR spectra for compound 223.

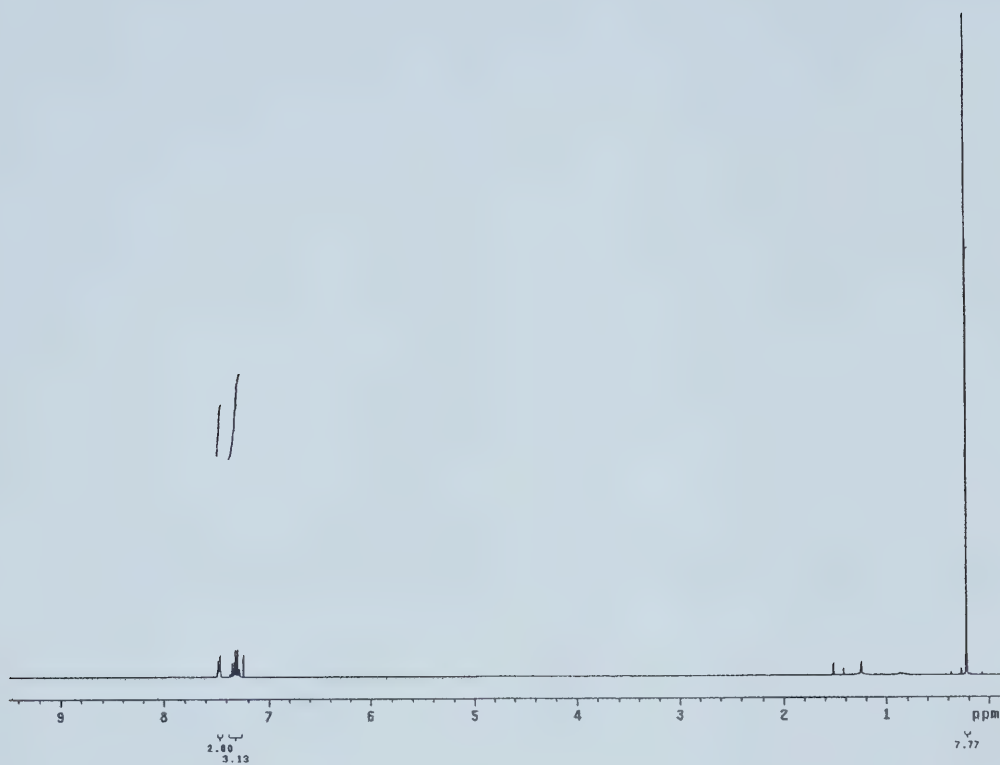


Figure B31. ^1H NMR spectrum for compounds **244** and **245**.

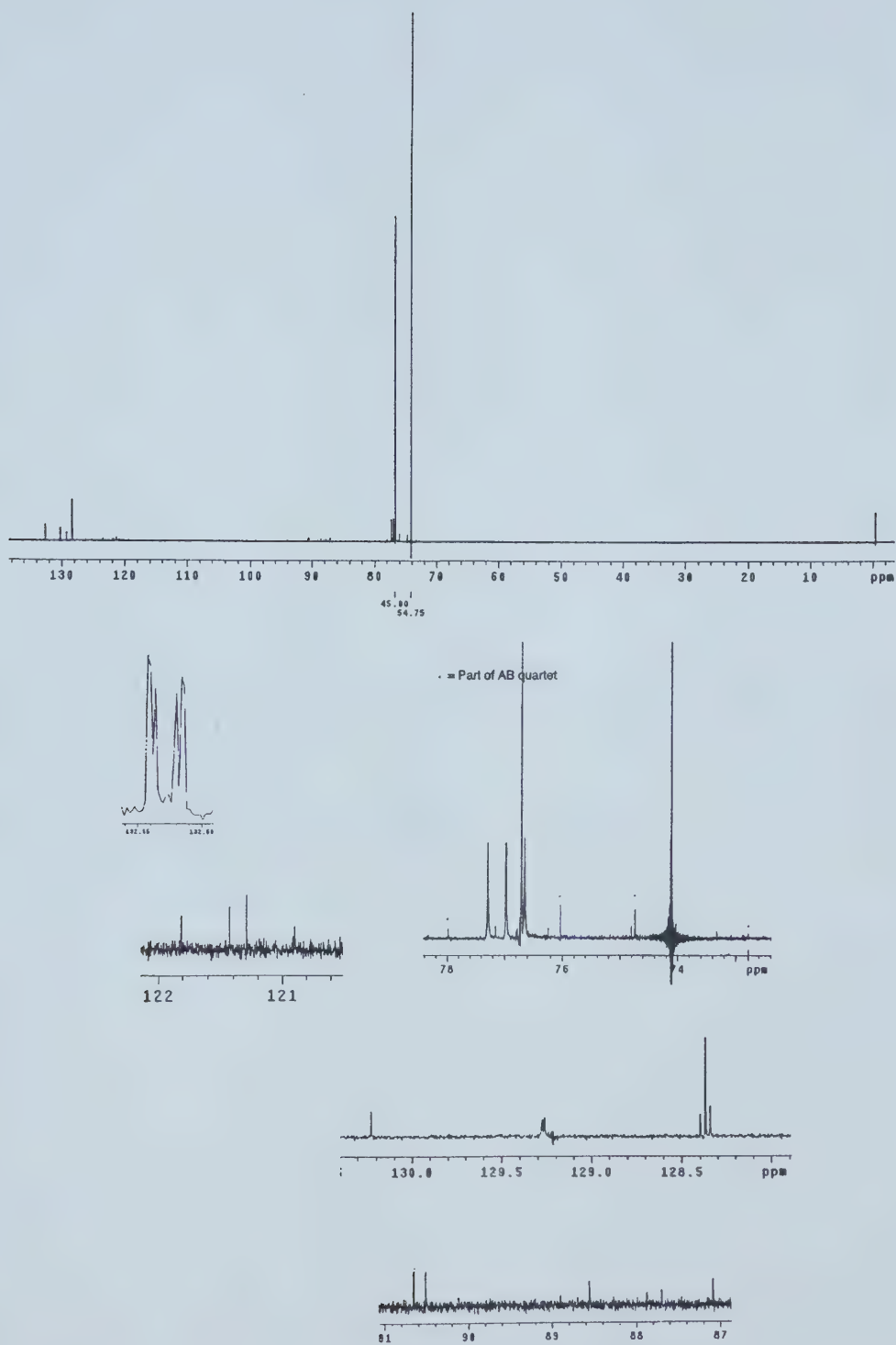
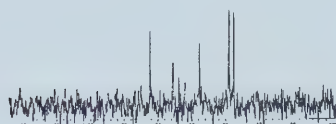
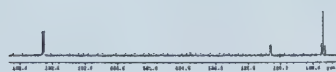
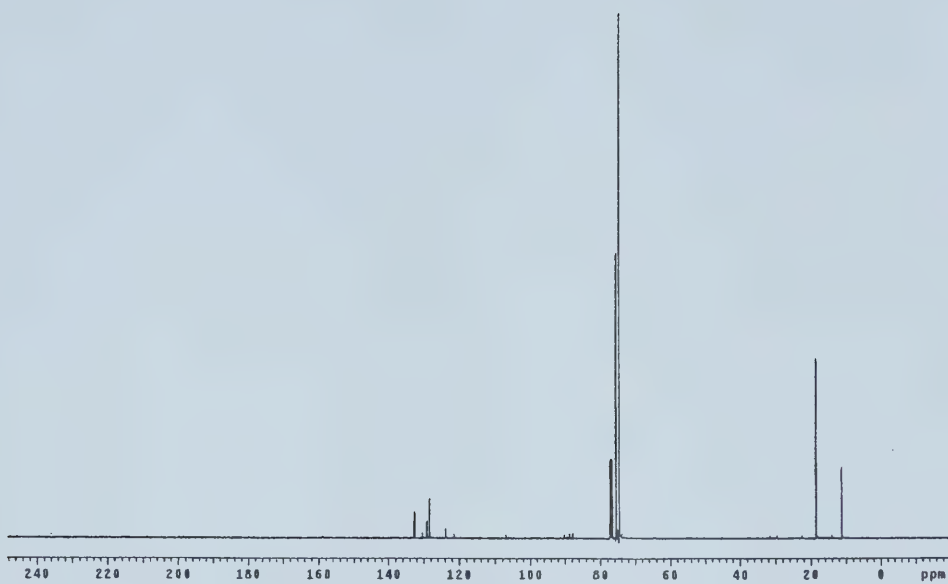


Figure B32. ^{13}C NMR spectra for compounds 244 and 245.



Figure B33. ^1H NMR spectrum for compounds 248 and 249.



≈ Part of AB quartet

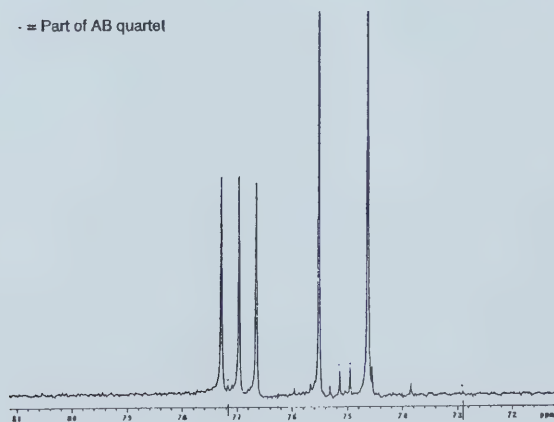


Figure B34. ^{13}C NMR spectra for compounds 248 and 249.



Figure B35. ^1H NMR spectrum for compounds 253 and 254.

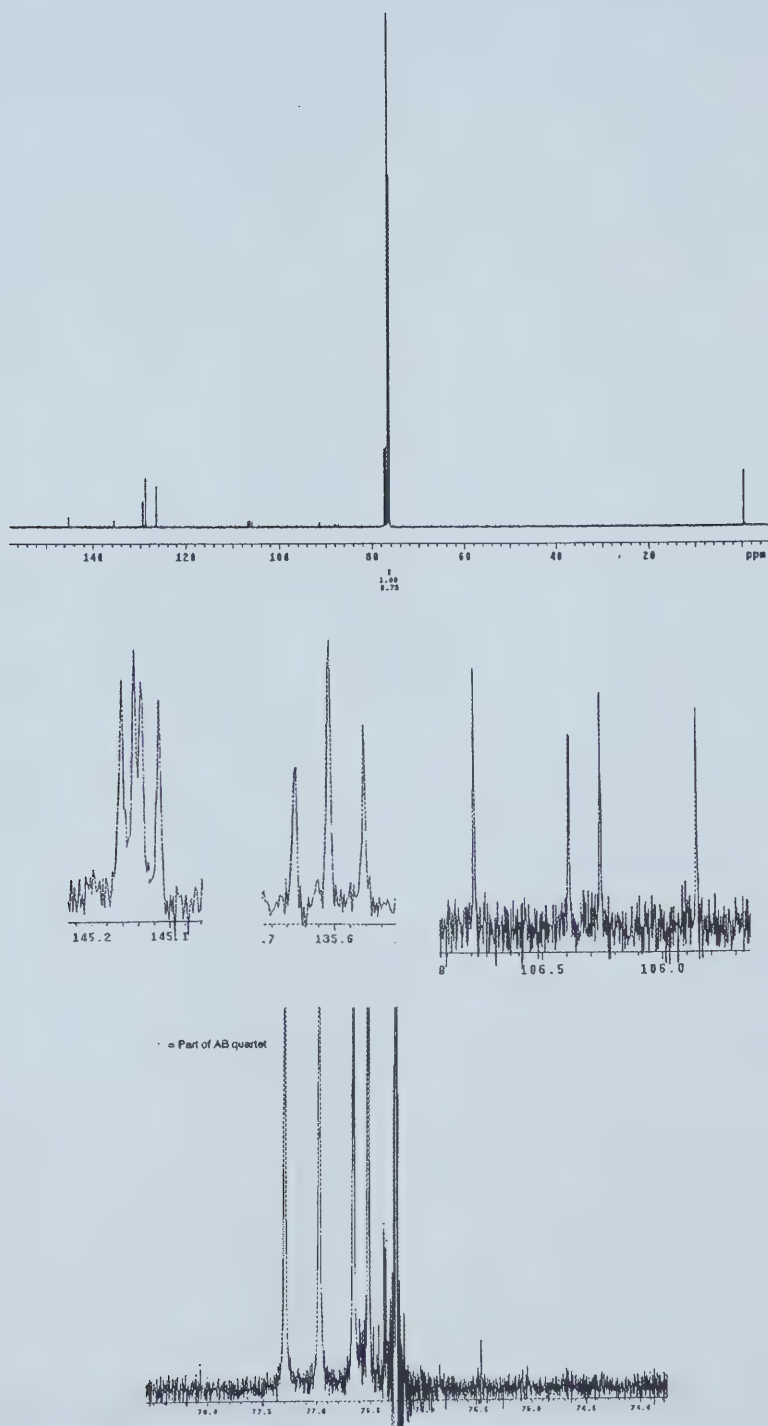


Figure B36. ^{13}C NMR spectra for compounds 253 and 254.

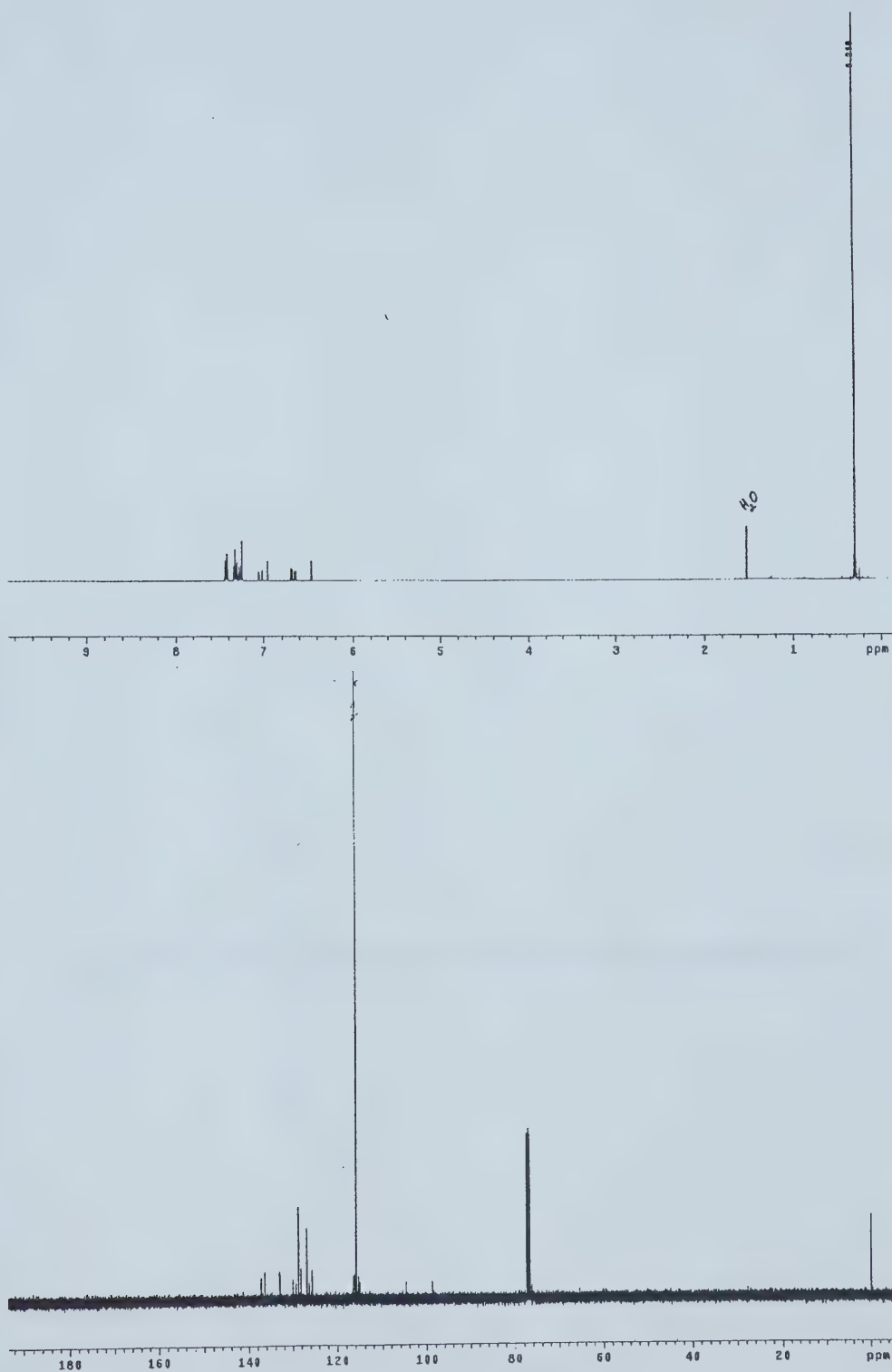


Figure B37. ^1H and ^{13}C NMR spectra for compound 255.



Figure B38. ^1H and ^{13}C NMR spectra for compound 259.



0 1620 1885 8355